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THE LANCET

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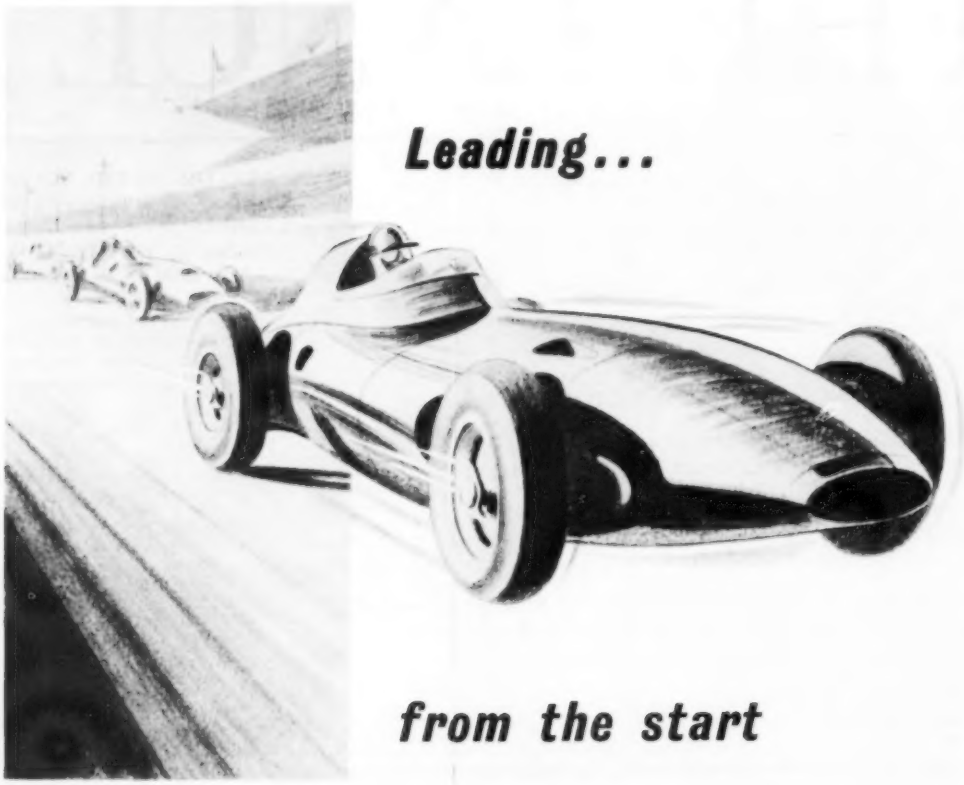

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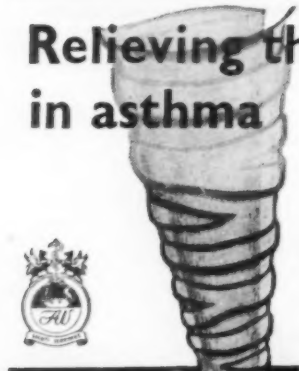

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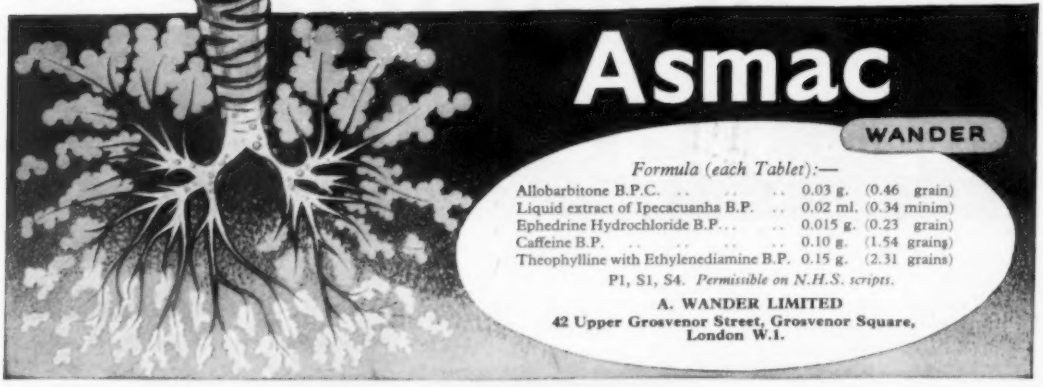

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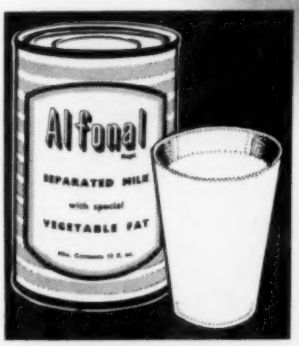

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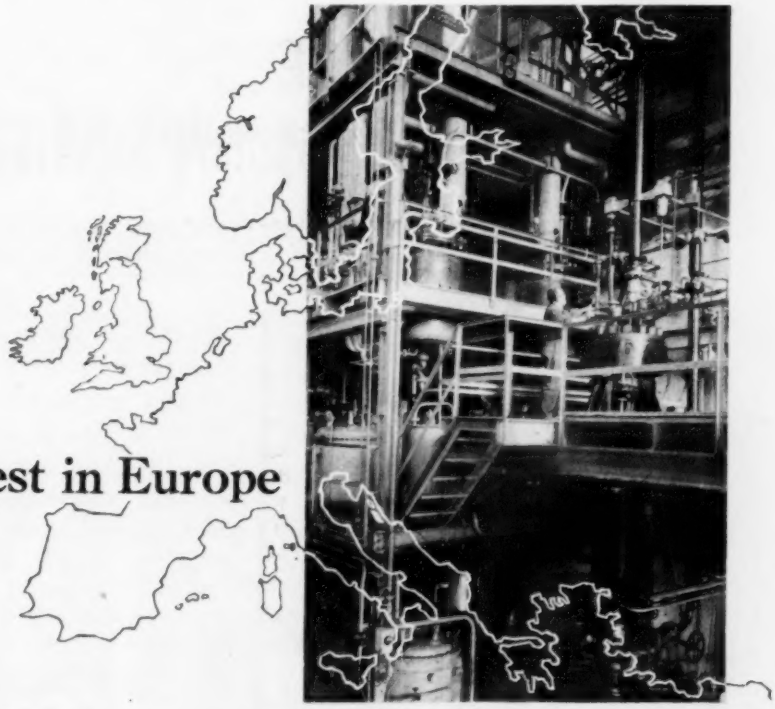

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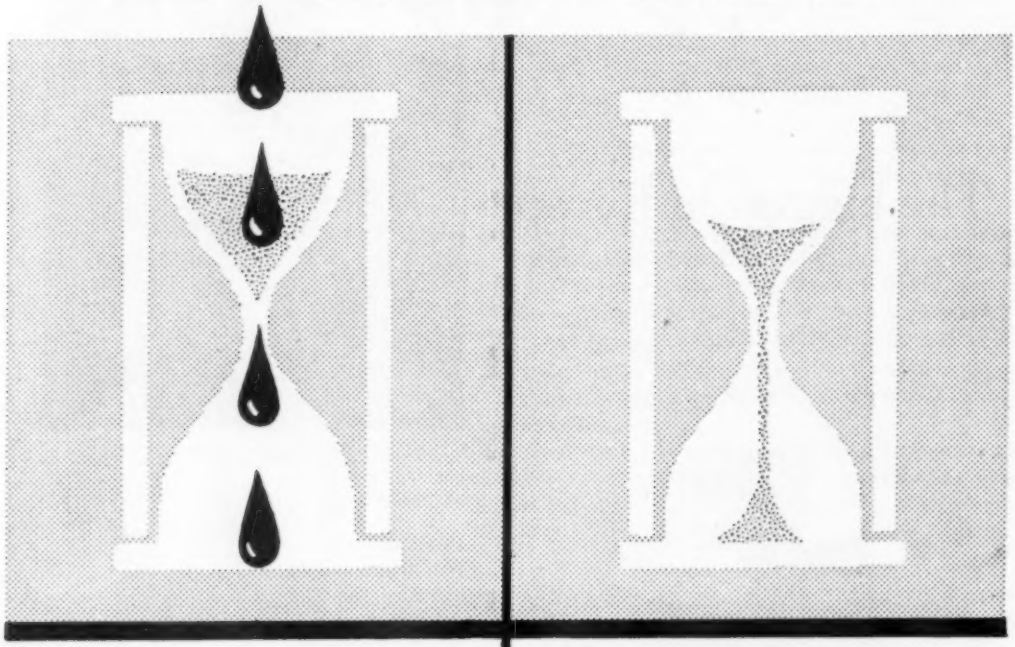

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Anaesthesia for Fractures of the Femoral neck. *Lancet* 1957, **1**, 1092
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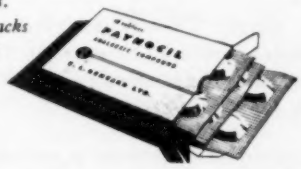

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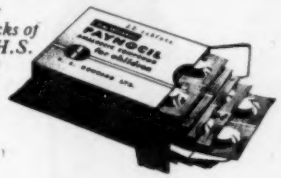

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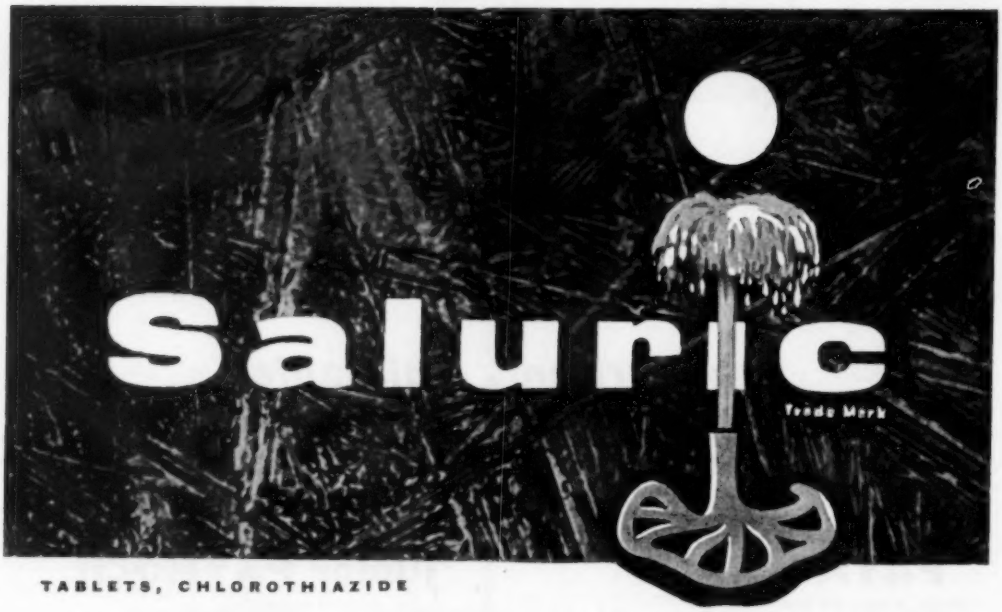

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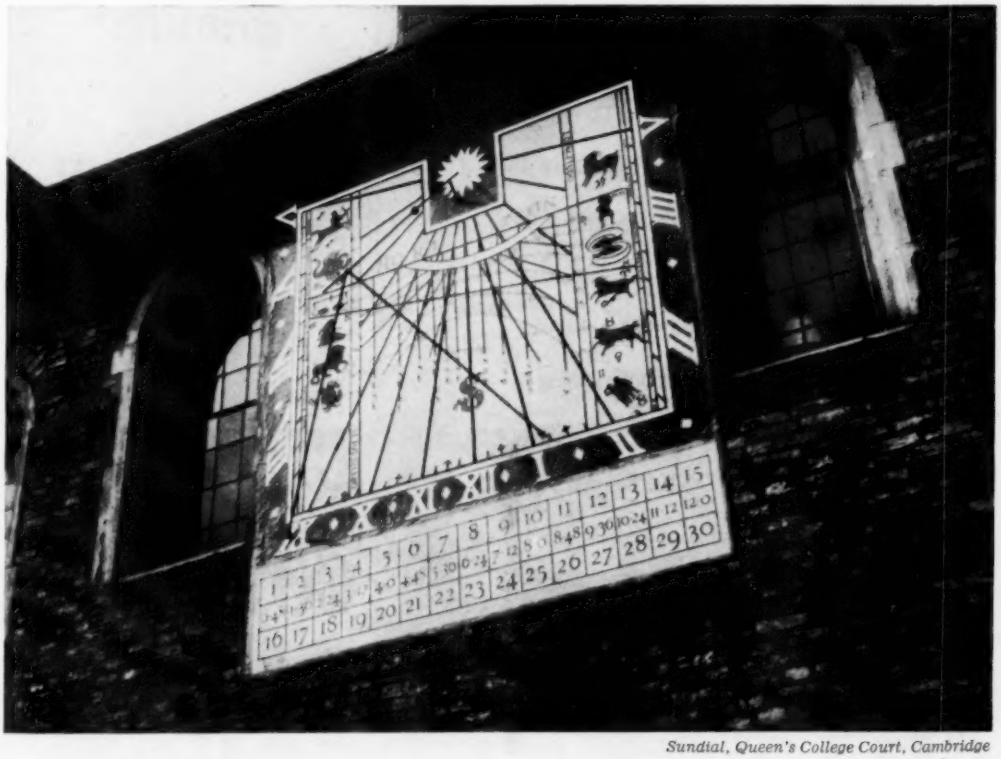

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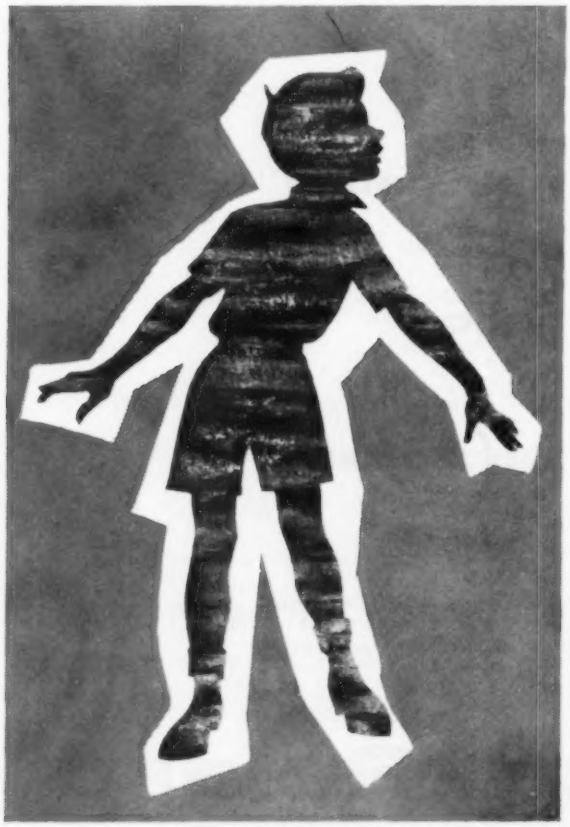

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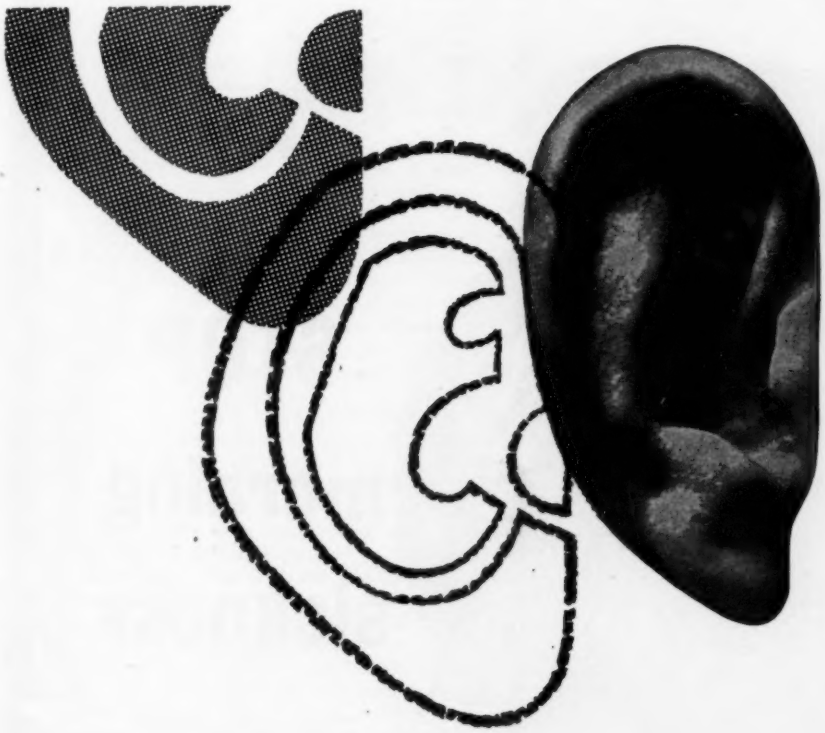

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CEREBRAL VASCULAR DISEASE IN THE LIGHT OF MODERN TECHNIQUES *

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CEREBRAL vascular disease is of great and, one fears, of still growing importance in Western society. It would be a fascinating historical study to examine the part it has played in the history of the last two thousand years with its stories of the gradual decline or perversion of powerful regimes and of the violent oscillations of events brought about by the sudden removal of some outstanding personality from the scene of human affairs.

Some idea of its importance in contemporary society can be obtained from a brief reference to the Registrar-General's Statistical Review for England and Wales in which the annual deaths from cerebral vascular disease over the ten-year period 1946-55 are compared with those from arteriosclerotic heart-disease and from carcinoma of the bronchus and lung—two disorders much in the public eye at the present time. Fig. 1 shows that the toll of cerebral vascular disease in every case surpassed that of the other two, and during the first half of the period exceeded their sum often by a considerable margin. American figures tell the same story. Wright and Luckey (1955) record that in 1952 there were 172,000 deaths from cerebral vascular disease—a figure exceeding by three times the combined deaths from diabetes and tuberculosis. These figures give no idea of the amount of chronic illness and of premature incapacity which, because of its nature, cerebral vascular disease inflicts upon society.

Old enemies, like old friends, are apt to be taken for granted and cerebral vascular disease is no exception. This is aptly illustrated by an extract from a clinical lecture published fifty years ago (Rose Bradford 1908). Speaking of cerebral aneurysms the lecturer said that these might give rise to no symptoms till they ruptured, adding: "These cases are of no clinical interest, they are merely cases of cerebral hæmorrhage". This statement cannot have seemed as unusual in those days as it does today, for twenty years later the speaker was president of this college.

It might be said that the last twenty years have not added greatly to our fundamental knowledge of cerebral vascular disease, but the developments in cerebral and vascular surgery and of surgical techniques, especially radiology, have thrown notable light on its details and have opened up new possibilities both in diagnosis and treatment. It is against this changing background that I propose to review the subject, selecting for particular discussion those aspects in which modern techniques have brought greater accuracy in diagnosis and are gradually bringing about a modification of orthodox attitudes towards management and treatment.

Classification

To have any hope of success an attempt to review so large a field requires a schema by which the subject may be broken down into manageable subsections; and, while being fully aware of its scientific imperfections, I propose to employ the following classification. It will be understood that in any individual patient more than one variant of cerebral vascular disease may exist at the same time.

Diffuse
(*a*) Generalised ischæmic brain degeneration from atherosclerosis.
(*b*) Cerebral disorder in arterial hypertension.

Local
(*a*) Focal softenings from ischæmia, including occlusion of minor vessels by thrombosis or embolism.
(*b*) Massive softenings from ischæmia, including occlusion of major vessels by thrombosis or embolism:
(1) Internal carotid artery occlusion.
(2) Basilar artery occlusion.
(*c*) Intracranial hæmorrhage:
(1) Meningeal hæmorrhage:
(i) Extradural.
(ii) Subdural.
(iii) Subarachnoid.
(2) Intracerebral hæmorrhage.

Generalised Ischæmic Brain Disease from Atherosclerosis

Though diffuse ischæmic brain disease is quantitatively the most important manifestation of cerebral vascular disease it need occupy only a few moments of our time, for its features are well known and have hardly been affected by modern advances. It is essentially the end-result of atherosclerosis with or without hypertension and such occasional aggravating factors as alcohol or head injury.

In many cases it is a disorder of gradual progression but its course may be punctuated by outspoken vascular accidents of greater or less severity.

Its most striking feature is progressive mental deterioration. At first the gradual falling off of the individual's innate creative capacity and of his desire and ability to meet new situations, together with a closing in of the mental horizon and an increasing egoism, may seem to be no more than the natural effects of advancing years. Forgetfulness, first for recent and then for more remote events, loss of capacity for all but familiar intellectual activities, accentuation of the underlying qualities of the personality, mood changes, decrease in emotional stability, and periods of confusion mark its advance into the realm of the pathological. Finally, a state of profound dementia supervenes, differing only in detail from that seen in other conditions of generalised brain destruction. This is a picture well known to us all. We see it in the world around us. It may fall to the lot of any of us to detect its earliest manifestations in ourselves, though it must be admitted that loss of insight is amongst the earliest features of this insidious disorder.

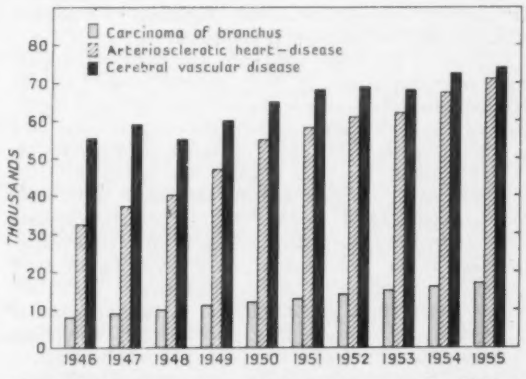

Fig. 1—Deaths from carcinoma of bronchus, arteriosclerotic heart-disease, and cerebral vascular disease in England and Wales, 1946–55.

* The first Lumleian lecture for 1958, delivered before the Royal College of Physicians of London on April 15.

Less familiar to many are the physical symptoms which may accompany and sometimes precede the mental change of diffuse ischæmic brain disease. Loss of physical agility may pass imperceptibly into lack of balance. The natural resilience of the gait is replaced by shuffling steps. The voice takes on a monotonous quality which is the prelude to a spastic dysarthria. Dyspraxia of the limbs and trunk adds its frustration to the effects of mental confusion and evokes outbursts of weeping or of laughter. Years of bedridden dependence upon others for the most elementary necessities of life may precede the patient's final release.

Such is a picture that has not changed through the centuries and which seems unlikely to change until we have some effective method of arresting arterial degeneration in general and atheroma in particular.

Cerebral Disorder in Arterial Hypertension

This interesting manifestation of cerebral vascular disease, often referred to as hypertensive encephalopathy, may be superimposed upon the background of ischæmic brain disease or may exist independently. It may occur in association with severe degrees of hypertension from whatever cause—e.g., in essential hypertension, unilateral renal disease, toxæmia of pregnancy, or rare disorders such as porphyria.

Its symptoms are both mental and physical, but these share in common a remarkable tendency to fluctuate in severity such as is seldom observed in other forms of vascular brain disease.

In the mental sphere, anxiety, confusion merging into delirium, and alterations of consciousness are more conspicuous than dementia. On the physical side, epileptic fits either generalised or focal are common. Manifestations of local brain dysfunction, such as blindness, loss of speech, and hemiplegia or monoplegia, having all the features of similar events due to vascular accidents, may suddenly make their appearance only to disappear in the course of a few days. Hypertensive retinopathy is commonly present, and varying degrees of hypertensive heart-failure may complicate the picture.

In spite of much that has been written, the underlying pathology of hypertensive encephalopathy remains obscure. If not directly dependent upon the degree of arterial hypertension, it is clearly closely related to this and as with retinopathy it is seldom seen with a diastolic pressure of less than 130 mm. Hg. The features of the mental picture suggest that we are here dealing with a diffuse process, while the focal symptoms indicate local involvement of portions of the brain. The rapid fluctuations in the severity of the symptoms both mental and physical can only be satisfactorily explained by a process which, at any rate initially, is reversible.

Œdema of the brain substance and nerve-cell anoxia from arteriolar spasm or from general slowing of the cerebral circulation suggest themselves as possible explanations. In hypertensive subjects the cerebral blood-flow is known to be significantly reduced. Denny-Brown (1951) believes that the changes are associated with multiple small cerebral lesions associated with small arterial occlusions. Pickering (1948) suggests that in cases of acute hypertension œdema of the brain is responsible, whereas in the hypertensive crises occurring in more chronic cases occlusion of small arteries is the cause. Foley (1956) finds the histological accompaniments of hypertensive encephalopathy to consist largely of swelling, miliary infarcts, petechial hæmorrhages, and evidence of increased vascular permeability, superimposed upon more chronic vascular lesions.

Whatever may ultimately prove to be the correct explanation of the phenomena of hypertensive encephalopathy, its general relationship to the level of the blood-pressure, and in particular to that of the diastolic blood-pressure, clearly demands that it should be given consideration in relation to the treatment of hypertension as a whole.

Much has been written in the past twenty years on the treatment of arterial hypertension. The era of thoracolumbar sympathectomy was followed by that of ganglion-blocking agents and of other drugs. Numerous series of cases have been published showing the effect of these procedures on the blood-pressure and on the patient's symptoms. No final conclusions can yet be drawn, and no doubt other hypotensive agents await discovery. In the series of cases published up to now relatively little reference is made to the effects of hypotensive therapy on the symptoms of hypertensive encephalopathy. These, admittedly, are more difficult to measure than the blood-pressure or the manifestations of cardiac embarrassment. But on the whole what comment there is seems to be unfavourable. Smirk and Alstad (1951) in their comparatively small series state that the incidence of encephalopathic attacks was not obviously altered. Shirley Smith (1954) and his colleagues go so far as to include " more than slight cerebral disorder " among the contraindications to the use of hexamethonium compounds. Graham and Maxwell (1954), on the other hand, include encephalopathy among their indications for urgent treatment.

My own impression has been more favourable to the value of hypotensive therapy in encephalopathy. In cases presenting primarily on account of cerebral symptoms it has seemed to me that effective lowering of the blood-pressure, however this is achieved, results in gratifying improvement both in the mental and the physical manifestations of encephalopathy; and I associate myself with those who take the view that even severe encephalopathy is a positive indication for hypotensive treatment, without committing myself to any final opinion as to which method of reducing the blood-pressure is to be preferred.

Focal Softenings from Ischæmia

The occurrence of " threatened " or " minor " strokes, often of a repetitive character, is a common event and in the past they have been attributed to the results of occlusion by thrombosis or embolism of the terminal branches of the cerebral vascular tree, to arterial spasm, or, in the presence of hypertension, to small hæmorrhages. In many cases this attribution is, no doubt, correct. The underlying pathology is diverse, and in conditions such as syphilis or infective endocarditis it may be amenable to direct curative treatment. But in the vast majority of such cases the underlying cause is atherosclerosis; and the patient's recovery depends upon the natural powers of readjustment, which are considerable. In the past, the degree to which the brain was supplied by end-arteries was overstressed, and Rosegay et al. (Rosegay and Welch 1954), among others, have demonstrated very clearly by angiographic studies the extent to which the collateral pial circulation from the anterior and posterior cerebral arteries may supply the area of cortex normally supplied by the middle cerebral artery when this vessel has become occluded.

It has long been known to pathologists that in brains examined after such incidents the extent of demonstrable infarction was often much smaller than might have been expected from the clinical symptoms, and that in a considerable proportion of cases of infarction the most careful

search has failed to reveal occlusion of the lumen of the artery supplying the damaged area.

These observations and the facts which have emerged as a result of the better recognition of the syndromes of occlusion of the carotid and basilar arteries, which will be considered later, have led Denny-Brown and his co-workers (Denny-Brown 1951, Meyer et al. 1956, Meyer and Denny-Brown 1957a and b) and later Corday et al. (1953, 1956) to postulate the state of "cerebral vascular insufficiency" as an alternative to "vasospasm", which has often been held to explain these occurrences. Denny-Brown defines "cerebral vascular insufficiency" in physiological terms as "a state of local or general cerebral blood flow that is unable to maintain the metabolic requirements of the brain during physiological stress". This state may be overt, leading to symptoms and signs during the stresses of normal life, or it may be latent and become manifest only as a result of some special stress—particularly an abrupt fall in the systemic blood-pressure.

The condition is the result of narrowing or occlusion, through organic changes, of the arteries—often at a point remote from their terminal distribution. This leads to the brain tissue becoming dependent for its blood-supply upon collateral branches from neighbouring vessels; this supply is adequate for ordinary purposes but falls below the critical requirement in the event of a sudden fall in the systemic blood-pressure or a further narrowing of the collateral vessel itself.

Denny-Brown and his associates have reproduced the clinical events observed in man in a series of beautiful experiments on monkeys after ligation of the common carotid or middle cerebral arteries.

Ligation of the middle cerebral artery under normal circumstances produces no demonstrable effects, the collateral circulation through the anterior and posterior cerebral arteries being fully adequate to maintain normal function. If, however, in such an animal the systemic blood-pressure was reduced by any means or the oxygen content of the blood diminished by breathing nitrogen a series of events was observed which closely paralleled those of a minor stroke. First, changes appeared in the electroencephalographic (E.E.G.) record of the effected area with failure of the normal electrocorticogram and the appearance of an injury potential, both changes, initially, being readily reversible. If, however, the hypoxic state was maintained stasis appeared in the smallest venules together with evidence of increased permeability of capillaries. Again these changes were initially reversible, but, if the anoxia were maintained, contiguous foci coalesced with the production of an irreversible infarct.

Denny-Brown and his colleagues conclude therefore that such infarcts are the result of tissue anoxia and that thrombosis of cortical vessels plays no part in their initial development.

USE OF ANTICOAGULANTS

The introduction during the past ten years or so of anticoagulant drugs suitable for prolonged administration has raised the question of whether these drugs have a useful part to play in the subsequent care of patients who have recovered from the effects of a minor stroke. Their value seems to be established in the immediate treatment of coronary artery occlusion, and many cardiologists advocate their continued and indefinite use in patients who have recovered from such an incident (e.g., Foley and Wright 1950, 1956, Wright 1955, Wright and McDevitt 1954).

However, the conditions in the heart and in the brain are not wholly comparable. The liability to an extension or an early recurrence of the occlusion is greater in the heart, whereas the risk of hæmorrhage into a softened area is peculiar to the brain. While recognising its risks and limitations, prolonged anticoagulant treatment is warmly advocated by Wright and his collaborators and by Millikan et al. (1955). In the nicely balanced conditions occurring in the brain the point can only be decided on a practical basis.

There would seem here to be an admirable opportunity for a properly controlled long-term investigation, which could only be adequately carried out in an institution caring for a large number of chronic sick and senile patients. Alternate cases considered to be at risk should be maintained on anticoagulants for the remainder of their lives and the occurrence of thromboembolic incidents estimated annually in both treated and untreated cases throughout their period of survival.

Occlusion of the Internal Carotid and Basilar Arteries

The brain receives its blood-supply from four arteries —the two internal carotids and the two vertebrals—the latter joining together to form the basilar.

The carotids and the basilar are of comparable size and are subject to the same disorders, of which atherosclerosis, aneurysm formation, and embolic occlusion are the chief. The three arteries enter into the formation of the circle of Willis, formed by the linking up of their terminal branches by the anterior and the two posterior communicating arteries.

In the normal and healthy subject this delicately arranged anastomosis serves to provide an alternative basic blood-supply to all parts of the brain so that either carotid and probably the basilar, provided it is only occluded over a short distance, can be eliminated without disastrous results. It has been shown by McDonald and Potter (1951) in the rabbit that the blood-flow through the posterior communicating arteries is normally zero, and that the same is probably true of the anterior communicating. The results of angiography suggest that the same is true in man so that in the normal, healthy subject the vascular fields supplied by the two carotids and the basilar remain distinct except at their periphery where they mingle at an arteriolar level.

But not all people are normal, nor are they all healthy. Congenital anomalies in the formation of the circle of Willis are common. Dandy (1944) stated that a "strictly normal" circle of Willis occurs only in 50% of cases. Defects in the posterior communicating arteries are especially frequent. Stopford (1916) found this vessel to be absent on one side in 6% and on both sides in 4% of specimens examined. Furthermore, the vessels entering into the formation of the circle are peculiarly prone to the premature changes of atheroma. Either type of defect, the congenital or the acquired, decreases the efficiency of the natural provision for an alternative blood-supply and increases the risk of disaster should any further occlusion take place. Catastrophe may be brought about by some event affecting the efficiency of the circulation as a whole, such as the lowering of the blood-pressure by a blood donation or by an attack of gastrointestinal hæmorrhage (Denny-Brown 1951).

Occlusion of the carotid or basilar arteries may be brought about by a variety of pathological processes; but the results are largely independent of the cause and are determined rather by the anatomical facts peculiar to the individual and by the general state of the cerebral circulation at the time. Embolism from any cause may be responsible. The carotid because of its length and its position may suffer from the results of trauma. Occasionally occlusion occurs in apparently healthy young people in whom the cause may remain undetermined. Such incidents are more commonly met with in the carotid than in the basilar artery.

Case 1.—A healthy young policeman, aged 24, attended

hospital on account of weakness and clumsiness of the right hand for two weeks. This had become apparent one day on parade when he found himself unable to carry out items of his drill requiring the use of the right hand. In retrospect he recalled that for several months he had been liable to drop things out of it. On examination at that time the only abnormal sign was loss of fine movement in the right hand with partial loss of postural sense and tactile discrimination in the fingers. General examination was negative. He made a complete recovery in a few weeks, and the diagnosis of disseminated sclerosis was thought most likely.

Some six months later while in Malaya he played a vigorous game of rugby football. During the following evening he felt generally unwell. After sleeping he woke suddenly in the morning feeling very ill and discovered that he was completely paralysed on the right side and was unable to speak.

After several weeks of mental confusion he was flown home where he was found to have a severe right hemiplegia, right hemisensory loss, and a right homonomous hemianopia. He had severe mixed dysphasia. General examination was still negative. A left carotid angiogram showed complete occlusion of the left internal carotid artery 1 cm. distal to the bifurcation of the common carotid artery.

No cause for this was found. Ten years later his general condition remains normal. The ætiology of the thrombosis remains unknown.

By far the commonest cause of occlusion both of the carotid and of the basilar arteries is atherosclerosis, and the patients are usually in the fifth or later decades of life.

Atheroma, though affecting major- and medium-sized arteries generally, has a special preference for certain sites among which the carotid, vertebral, and cerebral arteries are conspicuous. As has been so clearly shown by Hutchinson and Yates (1957), in any given case the carotid and vertebral systems are comparably affected and in considering the consequences of occlusion in either territory it is essential to bear in mind what may be taking place in the other. In short we have to accustom ourselves to thinking always in terms of caroticobasilar insufficiency. The same lesson is brought home by the results of both carotid and basilar angiography in atheromatous subjects.

Atherosclerosis affects the carotid and basilar arteries in several ways. Firstly, the arteries become tortuous and may eventually be subjected to such sharp kinking that relative stenosis of the lumen is brought about. Secondly, the weakening of the media may lead to aneurysm formation. Saccular aneurysms of the carotid artery in the cavernous sinus are relatively common, and fusiform aneurysms of the basilar artery are not very rare. Such aneurysms may undergo gradual thrombosis which may spread to the lumen of the artery or give rise to embolism in its branches.

Finally the intima of the vessel may become ulcerated with the development of a localised mural thrombosis, which in its turn may lead to a massive thrombosis and occasionally to embolism. This process of occlusion is often gradual, and cross sections of the artery may show lamination of the clot with recanalisation in its older parts.

Although in the respects that have been mentioned the carotid and basilar arteries are similarly affected and must always be considered in relation to one another, the syndromes that result from their final occlusion are sufficiently distinct for them to be considered separately.

INSUFFICIENCY AND OCCLUSION OF THE INTERNAL CAROTID ARTERY

The occurrence of massive occlusion of the internal carotid artery has been recognised for many years; but interest in it has been greatly stimulated in the past decade, largely as a result of the development of cerebral angiography. It is now recognised to be much commoner than would have been admitted ten years ago. In addition to isolated case-records, small collected series have been reported by Moniz and de Lacerda (1937), Gurdjian and Webster (1949, 1951), Elvidge and Werner (1951), Johnson and Walker (1951), Smyth (1954), Thomson (1954), Silversides (1954), and Shapiro and Peyton (1954).

The following brief account is based upon a study of the records of 32 cases who have been under the care either of myself or of my colleagues during the past five years, as well as of the reported cases. Published series show general agreement that the condition is commoner in males than in females in the proportion of about three to one, and that the left side is affected more commonly than the right in about the same ratio. My own figures are in agreement. The majority of the cases occur in the fifth, sixth, and seventh decades of life, but a significant number occur in young adults in their twenties and thirties; hence the average age of carotid occlusion is significantly lower than that of basilar occlusion. This extension into younger age-groups is partly accounted for by trauma, but in a considerable number the causation has remained in doubt. Antoni (1941) and Krayenbühl and Weber (1944) have attributed such cases to thromboangiitis obliterans, but none of their patients has shown evidence of this disease elsewhere in the body or any of the ætiological features characteristic of it. The majority of workers view the accuracy of this attribution with doubt.

There is general agreement that the principal ætiological factor is atherosclerosis, which may manifest itself in the early decades of life, particularly in the neighbourhood of the bifurcation of the common carotid artery.

The clinical picture of carotid thrombosis varies within wide limits.

At one extreme are the cases which present themselves in the form of massive contralateral hemiplegia coming on rapidly without warning and usually associated with depression or loss of consciousness. Gowers (1888) remarked on the relative rareness of such cases. If consciousness is sufficiently preserved, contralateral sensory disturbance and not infrequently homonomous hemianopia may be demonstrable. With a right hemiplegia severe dysphasia is the rule. Severe supraorbital headache may occur on the side of the diseased artery. Not uncommonly a unilateral or generalised convulsion heralds the onset. Blindness in the ipsilateral eye with narrowing of the retinal arteries and subsequent optic atrophy, although pathognomonic of carotid occlusion when it occurs, is relatively rare since the circulation through the ophthalmic artery is usually maintained either from the opposite internal carotid through the anterior communicating artery or by anastomosis with orbital branches of the external carotid. Occasionally papillœdema is present.

In patients who survive the immediate effects of the stroke, recovery sets in after a week or ten days and continues for many months. The hemiplegia shows considerable improvement especially in the leg, the arm remaining severely affected and the hand useless.

Where the major hemisphere has been damaged, the dysphasia improves but usually persists in some degree indefinitely, especially as regards spoken speech, and with it is found some mental deterioration and euphoria. Hemianopia may or may not persist, and if it does is likely to involve the lower more severely than the upper quadrants.

The picture thus comes to resemble that of occlusion of the middle cerebral artery, for which it is often mistaken. Subsequent angiograms of the unaffected carotid artery may demonstrate the filling of the anterior cerebral artery on the affected side through the anterior communicating artery.

Case 2.—A previously healthy man of 33, six weeks before admission, was given a tablet of 'Seconesin' on account of anxiety symptoms, to which he was subject. This was followed in fifteen minutes by wide-spread urticaria. He was given an injection of adrenaline which enabled him to go to sleep. Four hours later he had a fit in his sleep and on being woken next morning he was found to be drowsy, totally aphasic and paralysed on the right side of his body. When examined he was euphoric and still showed severe dysphasia. Vision and the visual fields were full. He had a right hemiplegia, complete in the upper limb and severe in the face and lower limb, together with slight general diminution of sensation on the right side of the body. General medical examination was negative. Blood-pressure 130/80 mm. Hg.

A left carotid angiogram showed complete occlusion of the internal carotid artery $^1/_2$ in. above the bifurcation of the common carotid. This was confirmed by operation.

Subsequently the patient's condition has improved somewhat.

At the other extreme carotid occlusion may cause no neurological symptoms at all. Such an occurrence, in a man dying of cancer, was recorded with expressions of surprise by Willis himself, who also noted that the patient had been troubled by severe headache on the opposite side of his head. It has long been known that in the majority of people surgical ligation of the internal carotid artery can be carried out with, at most, transient contralateral hemiparesis.

Under such circumstances the collateral circulation through the anterior and posterior communicating arteries must be sufficient to maintain normal function. As has already been said, congenital defects or degenerative changes in the circle of Willis may interfere with the efficiency of this compensating mechanism. The likelihood of hemiplegia occurring after carotid ligation thus increases with increasing age and is correspondingly lessened when the process of occlusion is gradual.

It is not possible to state with certainty what is the incidence of such symptomless thrombosis, but Hultquist (1942) found occlusion of one carotid in 4·4% of 1300 routine necropsies, and Fisher (1954) found complete occlusion in one or both internal carotids in 28 (6·5%) of 432 unselected necropsies.

Between these two extremes carotid occlusion more commonly shows itself in one of two recognisable clinical forms which may also occur in the presence of stenosis of the artery and before the lumen has become completely occluded.

The first, and by far the commonest, is that of transient episodes of unilateral disturbance recurring at irregular intervals over many months or years. For this syndrome Ramsay Hunt (1914) coined the appropriate phrase "cerebral intermittent claudication". Of these episodes the commonest is transitory numbness or weakness of one hand. Sometimes this will involve simultaneously the same side of the face or the whole half-body, and at other times the hemiplegia though transient may be complete.

The right side of the body is much the more commonly affected since the underlying change more often affects the left carotid, and right-sided attacks are usually associated with temporary loss of speech. Such aphasic attacks may be the sole symptom.

Other patients may report transitory loss or partial loss of vision in one eye, which may be mistaken for migraine—a mistake made easier by the common occurrence at the same time of unilateral headache.

Others may notice attacks of "dizziness", by which they mean a feeling of confusion and impairment of consciousness rather than of vertigo. Rarely, fits—focal or general—may occur.

Case 3.—A previously healthy man of 67 gave a history of four transitory attacks of weakness and numbness on the left side of the body in four weeks. The first episode came on without warning and consisted of sudden loss of power in the left hand and arm lasting only a few minutes. In subsequent attacks there was also numbness throughout the left half of the body. During the same period he noticed a tendency to bump into objects on his left and also rather severe intermittent headaches. On examination the only abnormal sign was a partial left homonomous quadrantic field defect. A right carotid angiogram showed complete occlusion of the right internal carotid artery.

The exact explanation of these transitory episodes was for some time disputed. They clearly could not be explained by thrombosis of the carotid artery as such since they might last only for seconds or minutes. The theory of "vasospasm" in the distal branches of the diseased artery has been much canvassed, especially by French and other Continental writers, on the analogy of the arterial spasm which has been observed to occur on puncture or other injury to the arterial wall. But direct evidence of such vasospasm was lacking, and such measures as stellate block or stripping of the nerve plexus in the adventitia of the artery have not, in the experience of most workers, proved successful in preventing such attacks. Some cases may be due to embolism into the distal branches of the affected carotid, but usually the attacks are too frequent, too stereotyped, and too transient to be explained on this basis.

The more satisfactory explanation is that of Denny-Brown who, as we have seen, believes them to be due to transitory ischæmia from failure of a collateral circulation which has hitherto maintained an adequate blood-flow in the distal branches of the occluded artery. He believes that the collateral circulation fails as a result of some decrease in the general cerebral circulation such as may follow a fall in the systemic blood-pressure or a decrease of the cardiac output from any of a wide variety of causes.

This explanation is the more satisfying since we now know that these attacks may occur in cases of carotid stenosis, before actual occlusion of the lumen has taken place, and since they have now been so exactly reproduced experimentally.

Finally, occlusion of the carotid artery may give rise to a gradually developing contralateral hemiplegia, initially most severe in the hand and face and often associated with dysphasia. In time the whole half-body is affected but the leg remains less damaged than the arm. In such cases focal or unilateral fits may occur, and headache on the side of the diseased artery may be severe. Such patients are usually thought to have a cerebral tumour, and it is during their routine investigation by angiography that a considerable number of the recorded cases of carotid occlusion have been discovered.

Case 4.—A woman of 50 was admitted for investigation because she was thought to have a cerebral tumour. Previously healthy, she was noticed some five months before admission to be becoming forgetful and apathetic. After some weeks she was reported to have had two seizures in one of which she became generally rigid and in the other she lost consciousness and shaking developed in the right arm and leg. Gradually a right hemiplegia developed, and a few days before admission her speech became disturbed and finally lost.

On examination she was drowsy and severely dysphasic. She had a right homonomous hemianopia without papilloedema,

and a right hemiplegia, complete in the upper limb and severe in the lower limb. General examination was negative. Blood-pressure 110/70 mm. Hg.

Ventriculography was first performed with negative findings. Bilateral carotid angiograms revealed thrombosis of the left internal carotid artery immediately distal to the origin of the posterior communicating artery. She survived and showed slight improvement in the severity of her hemiplegia.

Clinical Confirmation

In suspected cases of carotid occlusion the diagnosis can sometimes be confirmed by palpating the vessels in the neck (Ramsay Hunt 1914). If the common carotid artery is also involved absence of pulsation at the level of the bifurcation as well as in the superficial temporal and facial branches of the external carotid artery may be readily demonstrable. If the internal carotid artery only is involved the difference on the two sides may be detectable, but confusion with the external carotid artery and its major branches makes the test difficult to apply and unreliable in its results.

Palpation of the internal carotid artery from the pharynx (Gurdjian and Webster 1949) is a test most observers have found unsatisfactory. Decrease in the arterial blood-pressure in the optic fundus may be demonstrated by digital or instrumental pressure on the eye during ophthalmoscopic examination. Compression of the opposite carotid artery may be followed by immediate impairment of consciousness and if persisted in by convulsions, but this test should be used with restraint.

Absolute Confirmation

Absolute confirmation of the diagnosis can be made by carotid angiography or by surgical exploration. It is the development of the former technique that has revealed the relative commonness of carotid occlusion and of carotid stenosis and has stimulated contemporary interest in the subject.

The obstruction is usually at the level of the bifurcation of the common carotid or within 3 cm. above it (fig. 2). In 22 patients Thomson (1954) found this to be the case in 16 cases, 5 occurring in the carotid syphon and 1 in the common carotid artery.

In addition to the cases in which complete occlusion of the lumen is demonstrable, stenosis of the artery through the presence of an atheromatous area of the wall and a mural thrombus can sometimes be detected (fig. 3).

INSUFFICIENCY AND OCCLUSION OF THE BASILAR ARTERY

The results of occlusion of the basilar artery have much in common with those of occlusion of the carotid artery. Here, too, the important ætiological factors are embolism and atherosclerosis, the latter being much the more common. The average age at onset is higher than in the case of carotid occlusion. Cases of thrombosis below the age of 50 are rare. Interest in the subject was greatly stimulated by the paper of Kubik and Adams (1946) based on a clinico-pathological study of 18 cases examined at necropsy. But the clinical picture associated with basilar occlusion had long been recognised, as the following quotation will show:

" In occlusion of the whole basilar the limbs of both sides are usually affected. Sometimes at the same time, sometimes successively in the course of a few days. The limbs on one side, for instance, may become weak and improve; a day or two afterwards the other side becomes weak, and then there is again loss in the side first affected. The affection of the facial

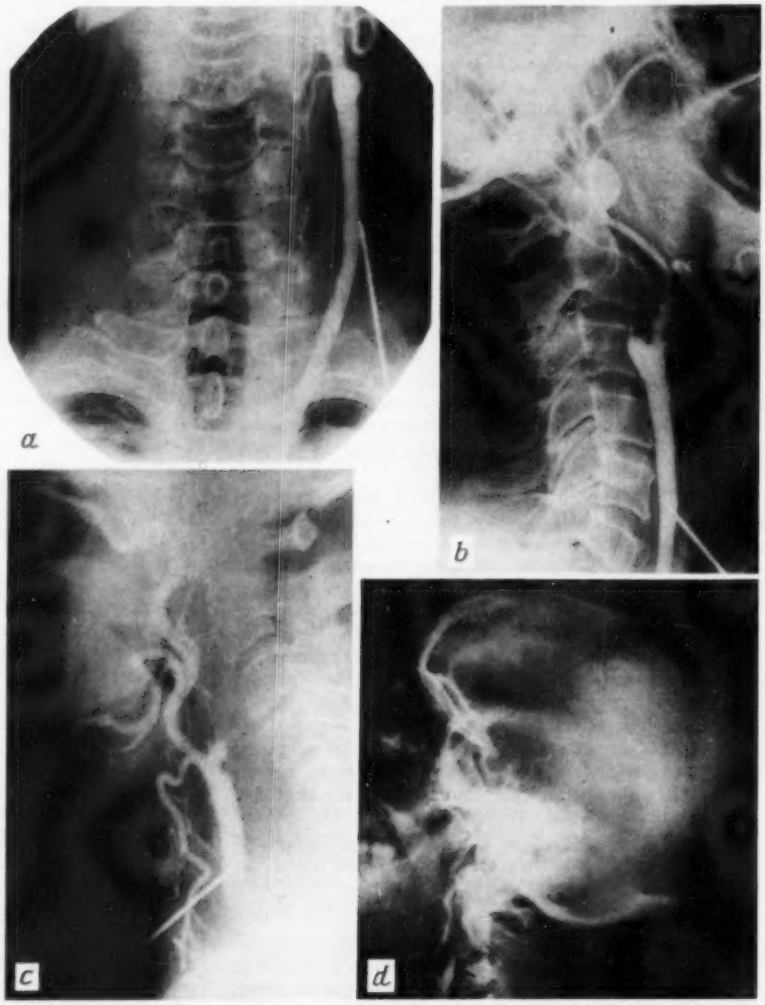

Fig. 2—Illustrative examples of occlusion of the internal carotid artery immediately distal to the carotid bifurcation: (*a*) in anteroposterior view; (*b*), (*c*) and (*d*) in lateral view.

or fifth nerve may present the same variations and often does not correspond to the affection of the limbs. There is usually considerable impairment of articulation and of swallowing. Loss of the conjugate movement of the eyes from palsy of external and internal recti is occasionally observed, with or without palsy of the facial nerve on the side of the affected external rectus. . . . When the obstruction involves the upper part of the vessel, as is usually the case in embolism, there are usually ocular symptoms other than conjugate deviation, ptosis, contracted or dilated pupils, with loss of reflex action to light, sometimes transient. There is occasionally paralysis of the whole or part of one third nerve or even of both. Less common is hemianopia, from extension of the clot along one posterior cerebral beyond the origin of the posterior communicating artery. Bilateral loss of sight, theoretically possible, is excessively rare. Obstruction of the lower extremity of the basilar is not common, except as an extension of a clot from one of the vertebral arteries. The onset of obstruction of the basilar artery is usually attended with a distinct apoplectic seizure, usually transient; it often recurs, and gradually deepens. The patient may lie for some days in a state of incomplete coma, can be roused to open his eyes, but does not speak. Convulsions occasionally attend the onset, but are on the whole not frequent; they may be general or partial; one limb or one side of the face may escape. Rigidity or clonic spasm in the legs or arms is much less common than in hæmorrhage into the pons."

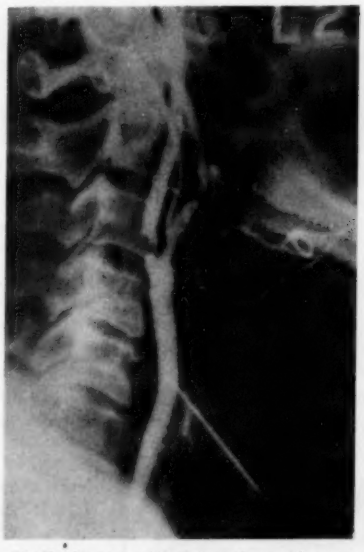

Fig. 3—Stenosis of the internal carotid artery from atheroma immediately distal to the carotid bifurcation.

This quotation is taken from Gowers' *Textbook of Nervous Diseases* (American edition) dated 1888, and could hardly be improved upon as a description of the clinical picture of massive basilar occlusion. Little needs to be added to it in the light of more recent knowledge, but a few comments may be made. The frequent depression or loss of consciousness, even in cases where the occipital lobes are not involved, is of especial interest with regard to the part played by brain-stem structures in the function of consciousness, which was till recently looked upon as dependent upon cortical activity. A symptom not mentioned by Gowers and now recognised as occurring in the majority of cases is severe headache, usually fronto-occipital. This is probably due to congestion of healthy vessels as a result of overloading of the collateral circulation.

Massive occlusion of the basilar artery is commonly fatal, but the period of survival varies over a wide range. In many of the reported cases the patient has died within two to three days of the onset of severe symptoms, while others have survived for from six to eight weeks. In less severe cases recovery may occur with varying degrees of residual disability, and, as will be seen later, such cases are probably more common than was previously recognised.

Case 5.—A man, aged 56, was admitted to hospital on March 1, 1956. Having previously been healthy he sustained, in 1942, a machine-gun wound of the spine which destroyed the spinal cord in its lumbosacral enlargement, rendering him totally and permanently paraplegic.

He made a good adjustment to his disability and led an active life as a school bursar, but developed a chronic urinary infection and was known to be hypertensive with blood-pressure around 230/130 mm. Hg. In November, 1955, he began to experience recurrent attacks in which for a few minutes he would feel faint and his sight would become blurred. Occasionally this blurring was associated with double vision. Three days before admission, having had such an episode in the morning, he was found by his wife some hours later unconscious in the lavatory. He was cyanosed and twitching on the left side of his body. He was admitted to hospital where it was observed that both arms were ataxic and that his speech was disturbed. Within a few hours he was unable to speak or to swallow.

When examined in the National Hospital on March 1, he was conscious but unable to speak. He could understand and obey simple commands and appeared to have normal fields of vision. Apart from the presence of nystagmus, his ocular movements were normal and the fifth-nerve functions were unimpaired. There was left facial weakness and the tongue deviated to the left on protrusion. As far as examination was possible he seemed to have a spastic weakness of the left arm and some ataxia of both but especially the left. Sensation above the waist was normal. The lower part of the body had the signs of complete transection of the cord in the upper lumbar region.

On the suspicion that the patient was suffering from thrombosis of the right internal carotid artery, a right carotid angiogram was done through the common carotid. This was normal except for some irregularity of the vessels suggesting atherosclerosis.

In the next two days the picture changed. Complete anarthria and aphagia were present. The respirations became periodic and the cough ineffective. Conjugate deviation of the eyes was lost. Both corneal reflexes disappeared and flaccid paralysis developed in the masticatory and facial muscles on both sides. Both arms were in a condition indicative of a double hemiplegia.

Basilar thrombosis was diagnosed and a vertebral angiogram performed (fig. 4) and reported on as follows: "A very small quantity of contrast medium is seen at the most superior part of the basilar artery in the lateral view; it is very thin and measures less than 1 mm. in diameter. In the anteroposterior view the left vertebral artery can be seen to be occluded 4·5 cm. from where it forms the basilar. This part of the artery has a beaded appearance. In the anteroposterior view also the proximal part of the basilar can be seen, and is also narrow and irregular. The appearances are very suggestive of a thrombosis of the left vertebral and basilar arteries."

As far as I am aware, this was the first occasion on which occlusion of the basilar artery was demonstrated angiographically during life. The patient died six weeks later.

At necropsy, in addition to cardiomegaly and the results of a longstanding paraplegia, there was widespread and advanced atherosclerosis. The basilar artery was dilated and tortuous and its lumen completely occluded by thrombus below the level of origin of the superior cerebellar arteries, the thrombus extending into the right vertebral artery as far as the mid-medullary level. This artery also showed several zones of incomplete obstruction in the neck. In addition there was complete obstruction of the left vertebral artery by thrombus for 2·5 cm. prior to its entry into the skull and a 50% reduction of its lumen thereafter. The common carotid arteries were atheromatous but not obstructed. The right internal carotid artery was atheromatous and about a quarter obstructed immediately distal to its origin. The left internal carotid artery

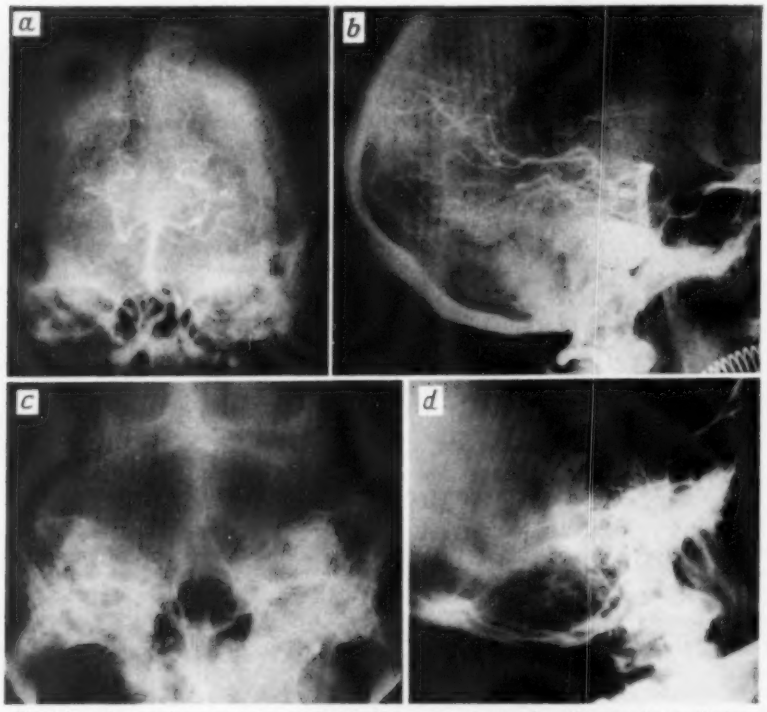

Fig. 4—Vertebral angiograms: (*a*) normal control in anteroposterior view; (*b*) normal control in lateral view; (*c*) case 5 in anteroposterior view, showing filling of the left vertebral artery with the basilar artery reduced to a thread and its branches unfilled; (*d*) case 5, the same in lateral view.

was almost completely obstructed just proximal to the carotid syphon. The circle of Willis was complete and the posterior communicating arteries were well developed. Areas of softening in the brain were of two groups, corresponding to an age of approximately seven weeks and of two days. The old lesions were present in the midbrain, pons, and medulla and in both lateral lobes of the cerebellum (fig. 5). There was also an area of softening in the right pulvinar, but the occipital lobes and calcarine areas were intact. The recent lesions consisted of recent infarction of the cortex supplied by the left middle cerebral artery and also in that supplied by the terminal branches of the left anterior cerebral artery. There was a similar area in the cortical zone supplied by the terminal branches of the left posterior cerebral artery.

It would appear that this patient had for a long time been virtually dependent upon the right internal carotid and left vertebral arteries for his cerebral blood-supply and had owed his survival to his well-developed circle of Willis and posterior communicating arteries. The occlusion of his basilar artery was the culminating disaster in a slowly developing sequence of events. Failure of the circulation in the terminal branches of his left middle cerebral, left anterior cerebral, and left posterior cerebral arteries were terminal events in the last few days of his life.

The importance of Kubik and Adams' (1946) paper lay, not so much in the fact that it described the clinical picture of fully developed basilar occlusion, though it certainly stimulated interest in it, as that, by careful retrospective correlation of the pathological findings with the history of the cases, it established that many of these patients had, for a considerable time, been having symptoms which, in the light of greater knowledge, could have led to the correct diagnosis being made before the final disaster. They thus made it clear that in many cases basilar insufficiency gives rise to transitory symptoms comparable with those in carotid occlusion. A similar conclusion was reached by Biemond (1951) from a careful study of 4 cases that came to necropsy.

The transitory symptoms in basilar insufficiency are of a nature that might be expected to arise from momentary failure of the circulation in structures normally supplied by its pontine and medullary branches and by the posterior cerebral artery on one or both sides. Commonly there are attacks of "dizziness", by which the patient usually means a feeling of faintness associated with a disturbance of balance though true vertigo may occur. There may also be tinnitus or momentary loss of speech. Numbness on one or both sides of the face may occur or paræthesiæ referred to one half of the body. Brief attacks of monoplegia or hemiplegia may be recorded. Transitory diplopia is common. Most significant of all are episodes of "dimness of vision" or "blackout" which may signify a transient hemianopia from ischæmia in the field of one posterior cerebral artery or of complete loss of vision if both are involved. In association with any of these symptoms headache, sometimes severe, may be experienced. Abnormal sensations referred to the abdomen may be noted. Frank cerebellar symptoms are rare, presumably because of the rich anastomosis between several vessels in this organ or because of its relative insensitivity to anoxia.

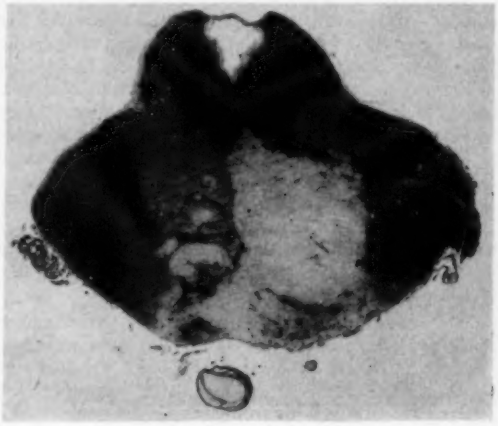

Fig. 5—Case 5, showing massive softening in the central area of the pons on the left side.

Case 6.—A 49-year-old master plumber, a known hypertensive and a heavy drinker who was found also to be diabetic, was admitted to hospital on account of attacks of numbness of the face over a period of four months. The first attack, occurring in a moment of annoyance, consisted of a feeling of "giddiness" with a sensation of pins-and-needles in both lips on both sides with numbness on the left side of the face, stiffening of the jaw and pulling of the tongue towards the left. He felt suddenly weak and found that he could not talk through stiffness of his tongue. When he tried to walk he staggered but there was no impairment of consciousness. In ten minutes he again felt normal. From their onset these incidents recurred at intervals varying from three days to three weeks with lessening intensity. Questioning elicited the fact that for three weeks he had experienced frequent sensations of sparkling lights passing from left to right in front of his eyes. Throughout the duration of his symptoms he had experienced severe left frontoparietal headaches.

Examination of the nervous system showed no abnormal signs. General examination showed evidence of mild diabetes, obesity, and considerable atherosclerosis. A right carotid angiogram was normal except for some increased tortuosity of arteries. A left vertebral angiogram showed normal filling of that artery, but the basilar artery was narrowed and irregular at its termination (fig. 6). The right vertebral artery was also filled and appeared irregular and narrowed. Anastomotic vessels were seen between the various cerebellar arteries. The film was interpreted as showing the presence of advanced atherosclerosis in both vertebral arteries and the basilar artery with almost complete occlusion of the right vertebral and of the basilar artery at its apex.

This patient continued to improve while in hospital and has remained well since, thus demonstrating that at least incomplete basilar occlusion may be compatible with relatively complete recovery. Numerous other examples in support of this contention might be quoted from recent hospital experience, but in the absence of arteriography or postmortem examination the diagnosis must remain presumptive. A similar view is held by Kubik and Adams (1946) and by Biemond (1951).

TREATMENT OF CAROTID AND BASILAR OCCLUSION

Management and treatment of carotid and basilar occlusion have many points in common and may be discussed briefly together.

Fig. 6—Vertebral angiogram in case 6 showing almost complete lack of contrast in the basilar artery and its branches.

In the presence of a major cerebral disaster following such an event, immediate treatment should be directed towards promoting the collateral circulation in the hope of minimising the extent of cerebral infarction. With this in view, nothing should be done to lower the systemic blood-pressure or to impair the vigour of the general circulation.

Attempts to increase the cerebral circulation have been made by the use of a variety of cerebral vasodilator procedures.

Of these, injection of the stellate ganglion or stripping of the adventitia of the carotid artery have been much advocated but are now little used, having been found to be without practical value as well as without sound physiological basis. The use of vasodilator drugs, such as papaverine and histamine, has proved of little worth, and it is notoriously difficult to increase the cerebral blood-flow by such means. The only physiological vasodilating agents are the products of metabolism, of which carbon dioxide is the most active; and the inspiration of 5% carbon dioxide in 95% oxygen for five minutes in every hour is probably the most rational way of promoting the opening up of the collateral circulation to a maximal extent.

The use of anticoagulants here, as in cases of vascular lesions involving the smaller vessels, is a matter of opinion and one requiring carefully controlled observation. When the diagnosis of carotid or basilar occlusion is established, and provided that the patient is not dangerously hypertensive, there seems to be a strong theoretical case for anticoagulant therapy. This is particularly true of cases in which transitory episodes are occurring but in which serious infarction has not yet taken place, as well as of cases due to embolism. In America the use of anticoagulants in such circumstances is certainly increasing.

In the longer-term management of cases of carotid occlusion we have nowadays to consider the possibilities of direct surgical intervention in the form of resection of a portion of the artery or of the removal of the clot followed by an attempt to re-establish the blood-flow with or without an arterial graft. Cases of this kind were reported by Strully et al. (1953), Eastcott, Pickering, and Rob (1954), and Edwards and Rob (1956).

Rob and Wheeler (1957) have recorded their experience of this procedure in 27 cases of carotid occlusion. Clearly with modern technical methods, including artificially induced hypothermia, the surgical procedure is not unduly hazardous. Satisfactory results can only be obtained before the thrombosis has extended into the intracranial portion of the artery, and as one might expect the best results are obtainable in those cases where the diagnosis has been made before irreversible changes have occurred in the brain, and particularly in cases of carotid stenosis.

This method of treatment cannot yet be applied to cases with comparable conditions in the basilar artery, but in view of the advances of the past twenty years it does not seem fantastic to hope that in due course methods may be found to overcome what at present seems an unsurmountable problem.

(*The references will appear at the end of the second lecture.*)

EXTRACORPOREAL CIRCULATION IN INTRACARDIAC SURGERY:

A COMPARISON BETWEEN TWO HEART-LUNG MACHINES

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IN many centres in the U.S.A. open heart surgery with the aid of heart-lung machines is undertaken almost daily. The very frequency and repetition of such operations has considerably reduced their risks, and in the less complicated cases their mortality-rate is now similar to that of other major surgical procedures.

In the pioneer stage fatalities could most often be attributed to the mechanical device. Subtle changes in the blood-clotting enzymes were common: pyrogenic surfaces, direct trauma to blood in turbulent pumps, inadequate flow or oxygenating capacity, and perhaps minute oxygen embolism all contributed to the early difficulties. But pump-oxygenators have improved, and several different models have been developed which cause less trauma to the blood and largely avoid the other difficulties. With the improved machines, the proficiency of the team has become relatively more important: their teamwork and experience begin to matter more than the choice of apparatus. Where open-heart surgery with a heart-lung machine has become a normal surgical procedure, morbidity and mortality depend chiefly on case-selection and surgical management.

At Stanford University Hospital during 1955–56 tests of several heart-lung machines established a preference for oxygenating the blood by surface filming rather than by introducing oxygen bubbles. Out of this study came the design of a machine using disposable plastic surfaces for oxygenation, in a modification of the principle advanced by Gibbon (1954). The Osborn machine (Osborn et al. 1957) was intended to have all the advantages of the Gibbon machine without its most serious disadvantage—i.e., the fact that surfaces which may be difficult to clean properly are repeatedly in contact with blood. The Osborn machine, together with a rotating-disc machine designed by Melrose (1955) at the Postgraduate Medical School of London, have been in routine clinical use since May of last year—the former throughout this period but the latter only since December. They have been operated by the same team and are at present used alternately. No particular selection of cases has been attempted save that when patients are large the Melrose machine is preferred because of its greater oxygenating capacity.

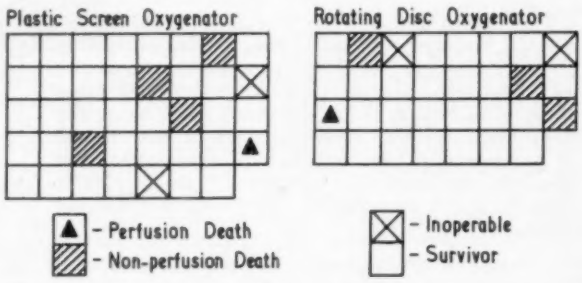
From a study of the 100 cases operated on during this time, no substantial difference in mortality or morbidity or any other measurable variable could be detected. As technique developed with experience, each machine could be expected to provide an entirely satisfactory operative environment, and the choice between them could thus be made only on grounds of convenience, cost per perfusion, and other administrative considerations.

On such grounds it has been decided to adopt the Melrose machine with an important change in its construction, so that all substantial parts in contact with blood may be made disposable and that they may be sterilised by autoclave. The oxygenator is to be of metal covered with 'Teflon', and disposable discs of stainless steel replace those now made of plastic. These requirements are judged essential for the proper maintenance and safety of an apparatus used more than five times a week. With this alteration, it is hoped that from now onwards this machine can be used for all intracardiac operations at Stanford University Hospital which require extracorporeal circulation of the blood.

Results of Operations

During the comparison of the two machines, 70 patients, in age between 4 months and 52 years and varying in size between 0·26 and 2·0 sq. metres, were operated on (table I). While the majority were in good health, there was no rigid exclusion of those not so fortunate. 3 were in heart-failure; 6 were undergoing a second or third thoracotomy; and pulmonary disease was present in several, as was marked cyanosis, which was extreme in 2. Though the acceptance of bad-risk patients is necessary, proper perspective is obtained only if, in the initial experience, they are interspersed with those offering a good chance of cure.

In presenting the results (see figure), we have followed



a format used by Kirklin et al. (1958), and like them have attempted to attribute to each death its true cause. Where no satisfactory clinical or pathological justification for the death was found, it was attributed to the perfusion. Some deaths have occurred in patients found to have lesions which defied correction. In the remainder, a review of the clinical course and necropsy findings showed sufficient cause to exonerate the perfusion. The figure shows this analysis. The mortality in this series is better than 19%, and when inoperable cases are excluded it is better than 13%.

The inoperable problems were a tumour of the left ventricle, the removal of which left too little muscular tissue to support life; 2 single ventricles which could not be anatomically divided and total anomalous pulmonary venous return in an infant. One of the 2 deaths attributed to perfusion was in a patient with an interventricular septal defect and moderate pulmonary hypertension. The other was in a patient with the tetralogy of Fallot who was markedly cyanotic. In neither could a satisfactory reason be given for their demise, one eighteen hours after operation and the other on the third postoperative day.

Among the causes found for failure in the remainder have been cardiac tamponade due to inadequate venting of the pericardium and retrosternal space, ineffective blood replacement during the postoperative period, and, in 1 case, massive infarc-

TABLE I—DISTRIBUTION BY ANATOMICAL DIAGNOSIS

—	No. of cases	No. surviving
Interventricular septal defect	20	17
Tetralogy of Fallot	14	11
Single ventricle	2	0
Interatrial septal defect (with associated conditions)	18	18
Left-ventricular/right-atrial shunt	5	5
Common atrioventricular canal	1	1
Total anomalous pulmonary venous return	1	0
Pulmonary stenosis	4	4
Pulmonary stenosis with atrial septal defect (cyanotic)	2	0
Mitral insufficiency	1	0
Left atrial tumour	1	1
Left ventricular tumour	1	0
Total	70	57

TABLE II—AVERAGE PLATELET-COUNT IN THOUSANDS

—	Plastic screens	Rotating discs
Before bypass	234	217
After bypass	144	130
One hour after bypass	175	165

tion of the right ventricle due to interference with its blood-supply. Heart-block has undoubtedly contributed in 2 instances but has not in itself been the reason for death. The presence of an unsuspected patent ductus arteriosus, in a patient operated on for interventricular septal defect, contributed to another failure. In this instance, equal pressures obtained both in the aorta and in the pulmonary artery which was enormously dilated.

Pulmonary complications have been little in evidence; and, save in the patient whose left ventricle, after the removal of a tumour, was deficient in muscular tissue, we have not been plagued by pulmonary œdema or abnormal bronchial secretions. Respiratory embarrassment occasioned by the thoracotomy has been greatly reduced by using the median stenotomy incision (Gerbode et al. 1958), and little difficulty attends convalescence on this score. We have noted, however, temporary respiratory acidosis when nursing care has not sufficiently encouraged breathing.

Post-perfusion Syndrome

We have not encountered "the syndrome of sudden death": no patient whose immediate postoperative condition was satisfactory deteriorated unexpectedly. More familiar has been a "post-perfusion syndrome", characterised by a persistent hypotension of mild degree, by restlessness and hyperpyrexia, and by mild cyanosis associated more obviously with the poverty of the peripheral circulation rather than with any respiratory cause. Review of the course of operation in the 5 patients with this syndrome has underlined the hypotensive element. Each was hypotensive during anæsthesia and surgery, even before perfusion was started. Neither blood-transfusion nor vasoconstrictor drugs had more than a temporary effect at this time.

During the period of perfusion, in spite of a perfusion-rate known to be adequate (2·3 litres per sq. m. per minute) the systolic blood-pressure remained below 70 mm. Hg and could not be raised by increasing the flow-rate. After perfusion the hypotensive state persisted. Errors in restoration of blood-volume were unlikely because the patients were accurately weighed after operation: 2 patients with this syndrome failed to survive and are classified as perfusion deaths; 2 others whose death is put down to surgical causes showed essentially similar signs; in another, these signs were of milder degree and progressively diminished, leading to full recovery. All were patients in whom considerable surgical correction was required; all had extensive refashioning of the pulmonary-outflow tract and each had a considerable return of blood from the open heart through bronchial-artery anastomoses. This latter problem is regarded as important, for blood collected from the open heart must undergo additional trauma, and embolism with air rather than with oxygen will be possible on its return to the extracorporeal circuit. That it should be returned is perhaps debatable, but certainly this is essential in all cases where such collaterals are prominent. It has been our policy to let such blood settle in a reservoir for as long as possible before returning it to the perfusion.

Elective Cardiac Arrest

Elective cardiac arrest with potassium citrate (Melrose et al. 1955) has been used routinely for defects involving the interventricular septum and whenever blood-loss has been excessive or has prevented a good view of the operative field. In this series, it has been used on 36 occasions. 2 patients have undergone repair of an interventricular septal defect twice, and on each occasion cardiac arrest was used. With necessary precautions (Gerbode and Melrose 1958) it is established that it is helpful, reliable, and safe.

The Hæmatology of Perfusion

Postoperative hæmorrhage has not been a problem, the average loss of blood being 890 ml. with extremes of 80 ml. and 4050 ml. 3 patients were reopened for such bleeding, and in 1 an obvious focus was found in the cardiotomy wound. The 2 others had undergone open heart surgery within the previous six weeks and both oozed considerably at the successful second operation. In each case evacuation of blood clots was followed by little further bleeding and full recovery.

Coagulation abnormalities have been slight and have required no unusual management. In routine investigations the following observations were made by one of us (H. A. P.).

In an attempt to compare the effect of the two types of pump oxygenators on the circulating blood, changes were followed in the levels of plasma-hæmoglobin, blood platelets, fibrinogen, and other plasma-coagulation factors. During the early part of this study, all the donor blood was approximately four hours old. More recent bypasses used blood collected twenty-four hours in advance. There was no difference in the hæmatological changes induced that could be ascribed to the age of the donor blood.

Fibrinogen loss, which was an important source of clotting difficulties with early experimental pump oxygenators (Osborn et al. 1956), did not occur with either the Osborn or the Melrose machine.

Platelet loss during the bypass occurred to the same degree with both (table II)—never to levels low enough to be responsible for hæmorrhage. After operation, the counts returned rapidly towards the control values in all but 2 cases, in both of which an unusual amount of bank blood had been given during the postoperative period because of surgical difficulties in securing adequate hæmostasis.

Plasma-hæmoglobin levels over 50 mg. per 100 ml. were unusual with either machine. Nor in most cases, could changes be detected in clotting-times, prothrombin-times, prothrombin-consumptions, or thromboplastin-generations. In a few cases, more pronounced rises in plasma-hæmoglobin, and definite changes in plasma-coagulation factors (especially those involved in the first stage of coagulation), did occur. These changes were correlated with the length of the bypass—and particularly with the amount of blood returned to the machine by suction from the interior of the heart—not with the type of machine used.

In no cases did a postoperative coagulation defect become a serious problem in management. Proper heparin neutralisation was ensured by a protamine titration technique (Perkins et al. 1956). Defects in plasma-coagulation factors (manifest most commonly by defective prothrombin-consumption) proved to be spontaneously reversible in a few hours, requiring no therapy beyond replacement of blood as it was lost. In cases requiring more than the average amount of blood post-operatively, persistent thrombocytopenia was prevented by using fresh plastic bag or siliconed bottle blood (Jackson et al. 1956).

Electrolyte Balance

We have noted only minor changes in the serum-electrolytes and have not regarded these as significant. Although a slight acidosis and lowering of the carbon-dioxide content has been observed in the postoperative period, it has only very rarely needed correction. A slight increase in the lactic-acid content of the blood has also occasionally been found, but this can be accounted for by accumulation of lactic acid in the blood used to charge the machines.

Conclusions

Few surgical groups have had the opportunity of comparing two heart-lung machines used concurrently in clinical practice. At Stanford University Hospital such a comparison has underlined not the differences but the similarities between two machines very different in design. Each is capable of imitating closely the normal cardiac output and of providing adequate gas exchange even for a large man. Neither has occasioned significant alterations in either the chemistry or the constituents of the blood and no untoward coagulation difficulties attend their use. As an outcome of this comparison it has become possible to decide on one machine; and, for reasons of convenience, cost, and ease of management, an apparatus utilising modified Melrose rotating-disc oxygenator is to be substituted for the present instruments.

Our experience lends support to the view that to improve the outlook for open heart surgery, improvement in team skill is more important than improvement in mechanical design. Until a disposable closed-circuit pump oxygenator of membrane type has been fully tested and has been proved to have the outstanding advantages it promises, present requirements can be adequately met with existing machines. We are convinced, however, that the most satisfactory clinical course follows the perfusion that most nearly maintains homœostasis, and that the machine chosen should be able to do this in all circumstances.

A remarkable benign and uneventful postoperative picture is presented by most of those now undergoing such surgery. The use of the median stenotomy incision rather than a bilateral thoracotomy decreases operating time considerably, and it is rare indeed for such a case to take more than three hours. This reduction in operating time has proved as beneficial in intracardiac surgery as in any other branch.

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TOBACCO AMBLYOPIA: A CLINICAL MANIFESTATION OF VITAMIN-B_{12} DEFICIENCY

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SINCE tobacco amblyopia was first described by Beer (1817) there has been much discussion about its ætiology. By definition tobacco is a necessary factor, but why should only a few people who smoke get this amblyopia? We attempt to answer this question.

Tobacco amblyopia is commonest in middle-aged males: Traquair (1930) found extremes of 23 and 84 years and only 7 females in 1525 cases. The amount of tobacco smoked varies considerably: Usher (1927) and Traquair (1930) found an average weekly consumption of 3 oz., with extremes of $^1/_2$ oz. and 9 oz. Tobacco amblyopia usually affects persons who smoke strong pipe tobacco; cigars and cigarettes are seldom responsible. Most patients have smoked for many years: Nettleship (1887) found symptoms developing after a minimum of a year's smoking.

It is generally accepted that excessive consumption of alcohol tends to increase the incidence and severity of tobacco amblyopia.

Many workers have recognised the importance of the nutrition and general health of the patient (Mackenzie 1854, Traquair 1930, Greeves 1946, Evans 1946, Schepens 1946). It has been suggested that a deficiency of one or more members of the vitamin-B group may be an ætiological factor, and the response to vitamin-B complex and yeast has been studied (Shattuck 1928, Minot 1929, Carroll 1944); but these clinical trials have not convincingly shown that it is deficiency of vitamin-B complex that is the cause of tobacco amblyopia. In many cases smoking had been stopped; this alone improves most cases. Often the diet and drinking habits of the patients had been altered, and it is now known that yeast contains a small quantity of vitamin B_{12} (Peeler et al. 1951).

Duke-Elder (1954) noted that the injection of large doses of vitamin B_{12} was effective in tobacco amblyopia, even if smoking was continued. It was therefore decided to determine whether tobacco amblyopia could be regarded as one of the clinical manifestations of vitamin-B_{12} deficiency.

Method

In this series the criteria on which the diagnosis of tobacco amblyopia was based were as follows:

(1) The patient must be a smoker.

(2) A centrocæcal scotoma must be present.

(3) This scotoma must be horizontally oval, with a sloping edge and most easily detected by a reduced stimulus—i.e., with a red or a small white test object.

(4) The scotoma must be bilateral, though not necessarily equal on the two sides.

(5) The defect for colour must exceed that for white.

(6) There must be definite nuclei within that scotoma on the horizontal meridian.

(7) An impairment of the temporal colour field must exist within the 30° circle. (In the more advanced cases a similar defect is also seen to a small white test object.)

The visual fields were investigated by one of us only (A. J. A. M.) to ensure uniformity of technique.

During a twelve-month period 14 male patients with tobacco amblyopia were seen by us at the Bristol Eye Hospital. A history was taken from each patient and a complete clinical examination made. In addition each patient underwent a full blood examination, gastric analysis, liver-function tests, and measurement of the serum-vitamin-B_{12} level. It was also decided that biopsy of the sternal marrow should be undertaken in every patient with histamine-fast achlorhydria and evidence of neurological involvement, irrespective of whether or not anæmia was present.

A summary of the clinical and pathological findings in 14 cases of tobacco amblyopia and the response to treatment with cyanocobalamin is included in the accompanying table.

Results

Anæmia

The hæmoglobin level was less than 90% in 3 of the 14 patients with tobacco amblyopia.

2 of these patients (cases 1 and 2) had histamine-fast achlorhydria and a megaloblastic marrow and therefore could be described as having the retrobulbar neuritis of addisonian pernicious anæmia.

Case 1.—A man, aged 62, was initially seen at the Bristol Eye Hospital in June, 1956, with three months' history of failing vision. His visual acuity was right 6/24, left 6/18, and the fields were typical of tobacco amblyopia. He was advised to stop smoking immediately and was given oral vitamin B_1. In spite of this his vision slowly deteriorated.

CLINICAL AND PATHOLOGICAL FEATURES IN 14 MEN WITH TOBACCO AMBLYOPIA

Case no.	Age (yr.)	History of smoking (yr.)	Visual acuity		Histamine fast achlorhydria	Hb (%)	Blood-picture	Serum bilirubin (mg. per 100 ml.)	Glossitis	Neurological involvement*	Serum-vitamin-B_{12} level (μμg. per ml.)	Visual acuity after smoking stopped and oral vitamin-B complex given		Visual acuity after parenteral vitamin B_{12}		Remarks
			Rt.	Lt.								Rt.	Lt.	Rt.	Lt.	
1	62	35	6/24	6/18								6/60	2/60			Deterioration of visual acuity followed cessation of smoking and treatment with oral vitamin B_1
	63	36	6/60	2/60	No acid	86	Normocytic normochromic film; megaloblastic marrow	0·2	+	+	15			6/9	6/9	After 5 mos'. treatment with parenteral vitamin B_{12} the fields, which were typical of tobacco amblyopia, including the nuclei, had almost returned to normal
2	75	—	6/6	6/6	No acid	33	Megaloblastic	0·7	+	—						Treated with anahæmin
	77	1½	6/60	6/60		93	Normal peripheral blood		—	—	130			6/12	6/9	Visual acuity and fields much improved after treatment with vitamin B_{12} for 2 mos.
3	81	50+	6/24	6/18	Free acid	89	Normocytic normochromic film; normoblastic marrow	2·75	+	+	300			6/9	6/9	Continued smoking; fields reverted to normal in 2 mos.
4	66	50	6/60	6/24	Refused gastric analysis	110	Normal film (refused marrow biopsy)	0·9	—	+	230			Failed to attend		—
5	78	60	6/9	6/24	Free acid	102	Normal	0·45	—	+	330	6/9	6/24	6/9	6/24	Choroidal sclerosis; field typical of tobacco amblyopia. Reverted to normal after treatment with B_{12}
6	52	30	6/36	6/36	Free acid	112	Normal	1·8	—	+	15	6/9	6/6	6/6	6/6	On vitamin-B complex and stopped smoking for 14 mos., yet right field still showed centrocæcal scotoma to red; fields reverted to normal after 2 mos'. treatment with vitamin B_{12}
7	65	50+	6/60	2/60	No acid	96	Normal	0·6†	+	—	220	6/24	2/60	6/12	6/24	Senile cataracts; stopped smoking and took vitamin-B complex for 17 mos., yet still tobacco amblyopia. After 4 mos'. treatment with vitamin B_{12} fields were normal in both eyes
8	72	55	3/60	2/60	No acid	114	Normal	0·95	+	—	300	6/60	6/60	6/9	6/9	Stopped smoking and took vitamin-B complex for 4 mos; fields normal after treatment with vitamin B_{12} for 3 mos.
9	64	50	6/24	6/24	No acid	113	Normal	0·4	—	—	350	6/6	6/9	Not given		Rt. field normal. Lt. field small centrocæcal scotoma to red 10 mos. after stopping smoking
10	66	45	6/9	6/24	No acid	107	Normal	0·35	—	—	220	6/9	6/12	6/6	6/9	Continued smoking with treatment; fields improved after 2 mos'. treatment with vitamin B_{12}
11	76	66	6/18	6/6	No acid	94	Normal	0·7	—	—	230	6/5	6/5	Not given		Fields normal 3 mos. after stopping smoking
12	60	40	6/18	6/9	No acid	99	Normal	0·65	—	—	200	6/6	6/6	Not given		Fields normal 6 mos. after stopping smoking
13	47	30	6/60	6/6	Free acid	96	Normal	0·45	—	—	300	6/6	6/5	Not given		Small centrocæcal scotomata to red in both eyes 4 mos. after stopping smoking
14	67	50+	6/60	Hand movements only	Free acid	104	Normal	1·35	—	—	Not done			6/36	Hand movements only	Stopped smoking and given vitamin B_{12}; visual fields returned to normal in 2 mos., advanced senile cataracts

* Neurological involvement, see text for full details.
† Serum-alkaline-phosphatase 16 King-Armstrong units per 100 ml.; serum-globulin 3·3 g. per 100 ml.

In March, 1957, he was admitted with three months' history of soreness of the tongue, slurring of speech, and numbness and paræsthesiæ in both legs. His visual acuity was right 6/60, left 2/60. The fields were now difficult to map accurately owing to poor fixation but showed a large centrocæcal scotoma to 3/1000 white on the right and to 15/1000 white on the left, with gross depression of the temporal fields to 15/1000 red. The tongue was smooth and red at the edges. There was impaired sensation to pinprick in both legs below the knees and diminished sense of position and vibration in the feet.

The hæmoglobin level was 86%; the serum-vitamin-B_{12} level was 15 $\mu\mu$g. per ml. Parenteral administration of cyanocobalamin 100 μg. daily for fourteen days followed by 100 μg. twice a week produced a dramatic improvement in the vision. Two months after treatment had been started the visual acuity was right 6/24, left 6/12, and the patient now had classical tobacco-amblyopia fields. His vision in both eyes improved to 6/12 in three months and 6/9 in six months.

Comment.—It seems reasonable to suggest that the tobacco amblyopia in case 1 can be regarded as a clinical manifestation of vitamin-B_{12} deficiency. The deterioration of vision and the defect in the visual field preceded the onset of anæmia, glossitis, and neurological involvement by more than nine months. The excellent response to parenteral vitamin B_{12} further supports the view that a combination of the toxic effect of tobacco on the retina and the low serum-vitamin-B_{12} level produced tobacco amblyopia.

Case 2.—A man, aged 75, was admitted to Southmead Hospital in August, 1956, under the care of Dr. J. A. Birrell with pernicious anæmia. He was treated with 'Anahæmin', and on discharge his hæmoglobin had increased from 33 to 70%.

In February, 1958, he attended the Bristol Eye Hospital with four weeks' history of failing vision. He had started smoking a pipe sixteen months previously. His visual acuity was 6/60 in each eye, and he had tobacco-amblyopia fields. No other abnormal physical signs were present. For the past eighteen months he had been having anahæmin 2 ml. twice weekly. His hæmoglobin level was now 93% and serum-vitamin-B_{12} level 130 $\mu\mu$g. per ml. He was given parenteral cyanocobalamin 100 $\mu\mu$g. twice weekly and allowed to continue smoking; within two months his vision had improved to right 6/12, left 6/9.

Comment.—It is evident that, in this known case of treated pernicious anæmia, vitamin-B_{12} deficiency was not sufficient to produce anæmia or signs of peripheral neuropathy or spinal-cord involvement. However, as in case 1, it seems reasonable to presume that the retina had been made unduly sensitive to vitamin-B_{12} deficiency. This hypothesis is supported by the knowledge that there was no amblyopia when the patient was very anæmic (Hb 33%), and at that time he was a non-smoker.

In case 3 neurological features suggesting vitamin-B_{12} deficiency were present, but there was free acid in the gastric juice, biopsy of the marrow showed normoblastic erythropoiesis, and there was biochemical evidence of liver dysfunction:

Case 3.—A man, aged 81, had six months' history of progressive deterioration of vision. For about two months he had had a sore tongue, numbness and tingling in his hands and feet, weakness of his legs, and difficulty in walking.

On examination his visual acuity was right 6/24, left 6/18, and the fields were typical of tobacco amblyopia. His tongue was red and smooth. His gait was a little unsteady. He had a definitely weak grip and some loss of power in both legs. Stocking anæsthesia to light touch and pinprick was present in both legs below the knees, and their sense of position and vibration was impaired. The knee-jerks were diminished, the ankle-jerks absent, and the plantar responses flexor. The hæmoglobin was 89%. A blood-film showed normocytic normochromic blood with anisocytosis and poikilocytosis. Gastric analysis revealed free acid, and the marrow was normoblastic. The serum-bilirubin level was 2·75 mg. per 100 ml. and the serum-vitamin-B_{12} level 300 $\mu\mu$g. per ml. The Wassermann reaction was negative.

Comment.—Case 3 had clinical manifestations of vitamin-B_{12} deficiency: glossitis, peripheral neuropathy, and involvement of the posterior spinal column. Within two months of parenteral administration of cyanocobalamin the visual acuity had improved to 6/9 in both eyes and the fields had become normal. This dramatic response can be entirely attributed to cyanocobalamin because the patient continued to smoke as heavily as before throughout the course of treatment.

Neurological Involvement

Clinical evidence of peripheral neuropathy, spinal-cord involvement, or encephalopathy was present in 5 of the 14 cases. Case 1 had pernicious anæmia. In case 4 the clinical picture strongly suggested subacute combined degeneration of the cord, but unfortunately the patient refused permission for full investigation and has repeatedly failed to attend for follow-up examination.

In the remaining 3 patients with neurological features suggesting vitamin-B_{12} deficiency gastric analysis revealed free acid. The findings of peripheral neuropathy and involvement of the posterior column in case 3 have already been reviewed. In case 5 there was six months' history of paræsthesiæ in both legs below the knees, but no abnormal signs were detected. The presentation of tobacco amblyopia and mental changes (acute depression, irritability, and failing memory for two months) in a non-anæmic patient (case 6) is of particular interest. Although free acid was present in the gastric juice, the serum-vitamin-B_{12} level was exceptionally low (15 $\mu\mu$g. per ml.) and liver-function tests showed a raised serum-bilirubin level.

Glossitis

A sore red smooth tongue was observed in 4 of our 14 patients. In 2 of these 4 the hæmoglobin level was below 90%; case 1 had pernicious anæmia; and case 3 had free acid and a normoblastic marrow. The 2 non-anæmic patients were forbidden to smoke and were initially given oral vitamin-B complex. This regime apparently produced no improvement in the state of the tongue. Treatment with cyanocobalamin caused complete subjective and objective improvement in the glossitis in all 4 patients.

Serum-vitamin-B_{12} Levels

The serum-vitamin-B_{12} levels were estimated by microbiological assay with *Euglena gracilis* var. *bacillaris* as test organism (Mollin and Ross 1952, 1954). With this method Mollin and Ross found that the normal range for serum-vitamin-B_{12} levels was 100–900 $\mu\mu$g. per ml., with a mean value of 360 $\mu\mu$g. per ml. The levels obtained in our patients with tobacco amblyopia were compared with those of a control group of healthy persons matched for sex and age.

In 13 patients with tobacco amblyopia the serum-vitamin-B_{12} levels ranged from 15 to 350 $\mu\mu$g. per ml., with a mean value of 218 $\mu\mu$g. per ml. The values for 12 controls ranged from 280 to 1000 $\mu\mu$g. per ml., with a mean value of 538 $\mu\mu$g. per ml. The difference in the serum-vitamin-B_{12} levels between the patients and the controls appears highly significant ($P<0·01$), according to the distribution-free type of test function used (the X-test by Van der Waerden). There is no significant

difference in age between the two groups by the same test function.

Treatment with Cyanocobalamin

Most cases of tobacco amblyopia improve when the patient stops smoking, and many cases even when smoking is only reduced. In our series cases 11 and 12 were completely cured in this way, and 4 patients cases (6, 9, 10, and 13) were clinically cured although slight signs of tobacco amblyopia remained in their fields.

This method of treatment has disadvantages: it is irksome to the patient, and the recovery-rate varies. In 170 cases Griffith (1887) found an average recovery period of seventeen months, with extremes of three and forty-two months. In our small series case 11 recovered in three months, whereas case 7 had not recovered after seventeen months. Rarely the vision may deteriorate, as in case 1 and in 4% of Griffith's (1887) cases.

We gave cyanocobalamin to 9 patients, of whom 3 continued smoking as heavily as before. All recovered more rapidly than would have been expected with the prohibition of smoking and oral vitamin-B complex alone; 6 patients had initially had this orthodox treatment. Parenteral cyanocobalamin 100 μg. was first given once or twice weekly for a month (once a day for the first fourteen days to our anæmic patients), then every fortnight for two months, and finally at intervals of a month. Probably it is safe to stop treatment after six months, provided that the fields are normal and there is no evidence of addisonian pernicious anæmia or neurological involvement. Our experience in this clinical trial suggests that much larger doses of cyanocobalamin would have been even more rapidly effective.

Discussion

Tobacco Amblyopia, Vitamin-B_{12} Deficiency, and Histamine-fast Achlorhydria

Gastric analysis revealed histamine-fast achlorhydria in 9 of 15 patients with tobacco amblyopia described by Leishman (1952) and in 8 of 13 cases in the present survey. In these 8 cases the serum-vitamin-B_{12} levels ranged from 15 to 350 μμg. per ml., with a mean value of 208 μμg. per ml.

Histamine-fast achlorhydria is an essential feature of addisonian pernicious anæmia and may precede the onset of anæmia by many years (Hurst 1922, Meulengracht 1925). Callender and Denborough (1957) produce evidence that there is a " pre-pernicious-anæmia " state in which there is achlorhydria with gastric atrophy, poor absorption of vitamin B_{12} corrected by intrinsic factor, and a low or a low normal serum-vitamin-B_{12} level without symptoms of anæmia. 2 of Leishman's (1952) patients and 1 of ours (case 1) developed tobacco amblyopia many months before they were found to have pernicious anæmia. In view of this it seems likely that they were in the " pre-pernicious anæmia " state at the time. One of the manifestations of this state might therefore be tobacco amblyopia. Callender and Denborough refer to the inheritance of pernicious anæmia and the " pre-pernicious-anæmia " state : Nettleship suggested that tobacco amblyopia might have a genetic basis.

Mollin and Ross (1954) have shown that a critical level for vitamin-B_{12} deficiency is 100 μμg. per ml., and that above this level in the serum the marrow is normoblastic. Because a level of 100 μμg. per ml. is a critical level for the marrow, it does not necessarily follow that the same applies to the retina poisoned by tobacco. It may well be that about 250 μμg. per ml. is the critical level of serum-vitamin-B_{12} for the development of tobacco amblyopia. The level of free vitamin B_{12} in the serum might also be important in this context because presumably it is only the free vitamin B_{12} that can be immediately used by the retina. Unfortunately we could only estimate the level of total vitamin-B_{12} in the serum.

In view of the fact that 2 of our patients (cases 1 and 2) with tobacco amblyopia and 10 of 75 cases reviewed by Leishman (1952) were found to have pernicious anæmia, we decided to review the published cases of retrobulbar neuritis in pernicious anæmia (Cohen 1936, Box 1936, Hine 1936, Talbot 1936, Kampmeier and Jones 1938, Turner 1940, Benham 1951, Nelson and Weaver 1956).

A survey of these case-reports suggests that many of these patients with pernicious anæmia could be described as having tobacco amblyopia. Of 15 patients 9 were specifically reported as being smokers and 14 were males, yet the proportion of males to females in pernicious anæmia is usually given as 1 : 3. One of the characteristics of British and American males is that they tend to smoke pipes and cigarettes more than do females. Unfortunately most of the fields reported were incomplete; the central fields were not always recorded, and only Benham (1951) used a red object. However, centrocæcal scotomata were found in 6 cases, which suggests tobacco amblyopia. Turner (1940) noted that the development of amblyopia was not related to the degree of anæmia or to neurological involvement. Possibly it is related to the smoking habits of the patient, the retina being unduly sensitive to tobacco owing to vitamin-B_{12} deficiency. In retrobulbar neuritis of pernicious anæmia the histological findings in the optic nerves (Bickel 1914) appear to be similar to those observed in tobacco amblyopia (Duke-Elder 1954).

Vitamin-B_{12} Deficiency in Liver Dysfunction

Since free acid was present in the gastric juice in 5 of 13 patients with tobacco amblyopia in our series and in 9 of 15 patients in Leishman's (1952) series, it is evident that addisonian pernicious anæmia or the " pre-pernicious-anæmia " state cannot be regarded as the only condition predisposing to the development of tobacco amblyopia.

In our 14 cases there was no history or clinical evidence of liver disease in any patient. However, it is well known that portal cirrhosis may remain latent for many years, and that its incidence increases with age. Rolleston and McNee (1929) and McCartney (1933) reported that 52·1% and 35% of cases of cirrhosis of the liver found at necropsy had no history, symptoms, or signs of liver disease during life. In this clinically latent group even liver-function tests may be completely normal (Hetzel 1950).

In 6 of the 14 patients with tobacco amblyopia liver-function tests indicated some abnormality. There was a slight increase in the serum-globulin and serum-alkaline-phosphatase levels in 1 patient and a raised serum-bilirubin level in 5 patients. If the normal serum-bilirubin level is accepted as being 0·62 ± 0·25 mg. per 100 ml. (Schilling and Harris 1952), the serum-bilirubin levels were high in 5 cases (2·75, 1·8, 1·35, 0·95, and 0·9 mg. per 100 ml.). Both De Schweinitz and Edsall (1903) and Greeves (1946) also found evidence of liver dysfunction in some of their patients with tobacco amblyopia. In our two proved cases of addisonian pernicious anæmia the liver-function tests were normal, and similar findings were reported in 19 of 20 patients with untreated pernicious anæmia described by Schilling and Harris (1952).

Swendseid et al. (1957) found that, in cirrhosis, there is a greatly reduced level of vitamin B_{12} in the liver, the average value being 26 μg. per 100 g., whereas in healthy people of all age-groups there is an average of 70 μg. per 100 g. of wet tissues. Probably, therefore, in some cases of tobacco amblyopia there is a low level of vitamin B_{12} in the liver.

Vitamin B_{12} exists in the serum both free (when it can be utilised by the tissues) and bound to α-globulin. It has been shown (Lear et al. 1954, Jones and Mills 1955, Rachmilewitz et al. 1956, Mackay et al. 1957) that, in hepatic cirrhosis, there is a rise in the level of bound vitamin B_{12} and often a fall in that of free vitamin B_{12} in the serum and an increased urinary excretion of what is apparently free vitamin B_{12}. In a case of obstructive hepatic necrosis described by Mackay et al. (1957) very high levels of bound vitamin B_{12} were found in the serum. It is suggested that, in some cases, the liver releases a binding protein with a high avidity for vitamin B_{12} which would "mop up" any available free vitamin B_{12} and hold it in the blood-stream. If this were so, we suggest that there might be less free vitamin B_{12} available to the retina and hence, if the patient was a heavy cigarette smoker or a pipe smoker, an increased liability to tobacco amblyopia.

In view of these findings and suggestions it is unfortunate that the levels of free vitamin B_{12} in the serum of our patients with tobacco amblyopia could not be measured. In our 6 patients with abnormal liver-function tests the levels of total vitamin B_{12} in the serum ranged from 15 to 300 μμg. per ml., with a mean value of 213 μμg. The mean value in our healthy controls was 538 μμg. per ml.

Low Serum-vitamin-B_{12} Levels in Dietary Deficiency

It is well recognised that the serum-vitamin-B_{12} levels may be very low after partial or total gastrectomy and in association with the "blind loop" and malabsorption syndromes, diverticulosis of the small intestine, and treatment with anticonvulsants (Spray and Witts 1958). Friedenwald (1953) has also shown that diabetics have a tendency to vitamin-B_{12} deficiency; this then may explain the increased incidence of tobacco amblyopia in diabetics. Low serum-vitamin-B_{12} levels have also been reported in "vegans" who cannot absorb normal amounts of this vitamin. Badenoch (1954), Harrison et al. (1956), and Spray and Witts (1958) have described megaloblastic anæmia due to dietary deficiencies. A dietary deficiency of vitamin B_{12} may be present in some elderly men, particularly if they live alone. This deficiency might be expected to predispose towards the development of tobacco amblyopia long before producing megaloblastic anæmia or evidence of neurological involvement. The increased severity and frequency of tobacco amblyopia which Schepens (1946) found among mal-nourished Belgians could be explained in this way. Some of the complicated changes in the visual field of prisoners-of-war in the Far East may be due to a combined deficiency of vitamin B_1 and vitamin B_{12}, the former causing the central, and the latter, combined with smoking, causing the centrocæcal part of the scotoma (Livingston et al. 1946).

Conclusions

We have presented evidence that, in persons with even mild vitamin-B_{12} deficiency, the retina or the optic nerve is unduly sensitive to tobacco.

In a study of 13 patients with tobacco amblyopia the vitamin-B_{12} levels in the serum ranged from 15 to 350 μμg. per ml. These values differed significantly from those obtained in healthy controls, the mean level in our patients being 218 μμg. per ml. and that in the controls 538 μμg. per ml.

Other clinical manifestations of vitamin-B_{12} deficiency may be absent because, in pipe smokers and in heavy smokers of cigarettes, the amblyopia may precede the onset of anæmia, glossitis, neurological involvement, or megaloblastic bone-marrow by months or even years.

We have also produced evidence that tobacco amblyopia and the retrobulbar neuritis of addisonian pernicious anæmia may be one and the same condition.

An important additional finding is that, in 2 of our patients, tobacco amblyopia and neurological features suggesting vitamin-B_{12} deficiency were associated with free acid in the gastric juice, abnormal liver-function tests, and low serum-vitamin-B_{12} levels.

We therefore suggest that, in any case of unexplained peripheral neuropathy, myelopathy, or encephalopathy, especially if it is considered to be due to nutritional deficiency, the levels of total and of free vitamin-B_{12} in the serum should be measured, even if histamine-fast achlorhydria is not present.

Gastric analysis revealed free acid in 5 of 13 patients, and in 6 of 14 there was biochemical evidence of liver dysfunction.

In this limited clinical trial the effect of parenteral cyanocobalamin in improving visual acuity and completely reversing the changes in the visual field has been most encouraging, even if the use of tobacco is continued.

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MALIGNANT RENAL HYPERTENSION (WILSON-BYROM SYNDROME) CURED BY NEPHRECTOMY

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IT was predicted by Goldblatt (1948) that there would be many mistakes in the application to man of his classical experiments on renal hypertension in rats. He did not mean that constriction of a main renal artery was the cause of all hypertension in man but that the experimental application of his clamp would exactly reproduce the physiological state of the kidney in essential hypertension. He considered his experimental method to be the best suited to effect a state of abnormal physiology analogous to that caused by arteriolar sclerosis in the kidney—namely, reduction of intraglomerular capillary pressure and reduction of blood-flow to the nephron.

Wilson and Byrom (1939) described a type of malignant hypertension in rats that apparently had its origin in reduced renal blood-flow. During the next fifteen years they retested their theory, received confirmation from Blacket and Sellers (1951), and outlined (Wilson 1953) a syndrome of hypertension in rats which has the following clinical and pathological features:

(1) Hypertension is produced by artificial stenosis of the main renal artery to one kidney, the artery to the other kidney remaining intact.

(2) Encephalopathy eventually develops, often without uræmia.

(3) The resulting hypertension produces extrarenal vascular lesions closely resembling those seen in human malignant hypertension in all organs except the kidney supplied by the stenosed artery.

(4) Prompt removal of the kidney made ischæmic by the stenosis usually relieves the hypertension and is followed by disappearance of the encephalopathy.

(5) Histologically the excised kidney and its stenotic artery reveal no abnormality.

We report the following case for several reasons: the pathological findings responsible for the hypertension closely parallel Goldblatt's original experimental method; clinical and laboratory data were collected both before and after operation; and strong support is given to the suggestion that malignant hypertension may be due to renal factors.

Case-report

A weaver, aged 56, was admitted to this hospital on March 5, 1954, with several months' history of hypertension. His family doctor first diagnosed hypertension in June, 1953, when the patient's blood-pressure was 210/110 mm. Hg and nothing abnormal was found in his urine. Treatment with 'Metamine' (triethanolamine trinitrate biphosphate) was instituted. A few weeks later the patient had an attack of epigastric pain, hæmatemesis, and bitemporal headache. In December, 1954, his blood-pressure was 224/110 mm. Hg, and rales heard in his chest suggested a low-grade pulmonary infection. Albuminuria had also appeared. Antibiotics and digitalis procured the patient some benefit.

On admission to this hospital his blood-pressure was 216/130 mm. Hg in his right arm and 260/160 mm. Hg in his left. His cervical veins were distended. He had a conjunctival hæmorrhage, grade-IV retinopathy, papilloedema, and flame-shaped retinal hæmorrhages. His vision was much impaired. His heart was enlarged to percussion, and the edge of his liver was tender and palpable 8 cm. below his costal margin. His peripheral pulses were strong. His lungs were emphysematous but free from rales.

Investigation showed hæmoglobin 12 g. per 100 ml., white blood-cells 15,300 per c.mm., erythrocyte-sedimentation rate 28 mm. in 1st hour (Westergren) and urine sp. gr. 1·029, copious albumin, blood-urea nitrogen 22 mg. per 100 ml. The phenolsulphonphthalein test showed that 10% of the dye was excreted in the first 15 minutes and 25% after 2 hours. The retention of bromsulphalein was 20%. Radiography of the chest showed that the heart was enlarged transversely with prominence of the left ventricle and calcification of the aortic knob. The vascular markings of the lungs were consistent with early pulmonary congestion. Intravenous pyelography showed an enlarged right kidney with good concentration of the dye, whereas the left kidney could not be seen at all. There was calcification of the abdominal aorta and the iliac vessels. Electrocardiography showed left ventricular strain. Retrograde pyelography showed normal renal architecture bilaterally, but indigo-carmine injected intravenously was not excreted from the left kidney. The arm-to-tongue circulation-time was prolonged by 31 seconds. Lumbar puncture produced cerebrospinal fluid (C.S.F.) under a pressure of 216 mm. H_2O and containing protein 150 mg. per 100 ml. 'Regitine' reduced the blood-pressure from 254/150 to 210/110 mm. Hg.

Treatment and progress.—Clinically the patient became rapidly worse while being observed under the customary treatment. On the ninth day after admission his condition was desperate, and he lapsed into semicoma with Cheyne-Stokes respiration. Lumbar puncture produced C.S.F. under a pressure of 340 mm. H_2O, and the electroencephalogram was very abnormal. 50% glucose intravenously, hexamethonium, and hydrallazine were administered to improve his condition for surgery. His blood-pressure fell from 254/150 to 220/110–120 mm. Hg, the fall producing temporary improvement and mental clearing. An attempt at retrograde aortography failed.

Operation.—On March 17, 1954, under spinal anæsthesia, left nephrectomy was done, with resection of a segment of the left renal artery. At operation a pulseless renal artery and an apparently normal kidney confirmed the preoperative diagnosis of a Goldblatt kidney.

Pathology.—The operation specimen consisted of a section of stenosed renal artery, its lumen being reduced by 85% (fig. 1), and the left kidney (118 g.), whose capsule stripped easily. The cortex measured 4 mm. and the pyramids 11 mm. The mucosa of the renal pelvis was slightly hæmorrhagic. Microscopically the nephrovascular units were well preserved (fig. 2), arteries and arterioles being normal. Mild fibrous infiltration and lymphocytes were found in both the parenchyma and the capsule. A few tubules were dilated with either hyaline or protein casts. Microscopic sections of the

Fig. 1—Cross-section of renal artery at site of maximal stenosis. (Elastic-tissue stain.)

renal artery showed extensive fibrous proliferation of the intima. The elastic intima was distinct. Occasional focal infiltration of lymphocytes in the proliferating intimal layer gave the picture of acute inflammation. Unfortunately a biopsy specimen of the right kidney was not available to confirm feature no. 3 of the syndrome (see above). We believe that this case satisfies the criteria outlined by Homer Smith (1948) for cure of hypertension by nephrectomy.

Postoperative course.—Striking changes followed surgery. At the beginning of the operation the patient's blood-pressure was 250/150 mm. Hg, and at its end 210/110 mm. Hg. By 10 P.M. that evening it was 154/90 mm. Hg and by midnight 100/70 mm. Hg. When the electrocardiogram suggested myocardial ischæmia, noradrenaline was started by intravenous drip, and the blood-pressure rose to 180/100 mm. Hg. By March 24, five days after nephrectomy, the blood-pressure became steady at about 160/80 mm. Hg. There was never any evidence of surgical shock. By March 27 there had been spectacular improvement in the visual acuity of the left eye, and the papillœdema in the right eye had disappeared. The ophthalmologist considered the retinopathy to be grade IV on April 2, with corrected vision of 20/60 O.D., 20/20 O.S., and the capacity to read Jaeger-3 print. A week later the corrected vision was 20/20 O.U., and the patient could read Jaeger-1. Retinopathy was estimated at grade II on April 23. Lumbar puncture eleven days after the operation produced C.S.F. under a pressure of 100 mm. H_2O and containing protein 14 mg. per 100 ml., compared with 340 mm. H_2O and 150 mg. per 100 ml. preoperatively. By April 21 the urine contained no albumin. The blood-urea nitrogen was 26 mg. per 100 ml. four days before the operation, 17 mg. per 100 ml. by June, and 12 mg. per 100 ml. in December, 1954, and the urinary excretion of phenolsulphonphthalein had improved by August 24, 1954, to 40% in 15 minutes and 76% in 1 hour. A bromsulphalein test on admission showed that 20% of the dye was retained, but on April 2, 1955, only 6% was retained. The hæmoglobin increased to 14·6 g. per 100 ml. in August, 1954. On radiography the transverse diameter of the cardiac silhouette decreased to 143 mm. by April 5, 1955, the radiological signs of pulmonary congestive completely disappeared, and electrocardiography showed less signs of left ventricular strain. The preoperative electroencephalogram was interpreted as dysrhythmic, revealing many more frequencies of higher than average amplitude, especially in the frontal and central areas; these were described as consistent with disordered cerebral metabolism. On Sept. 14, 1955, electroencephalography showed remarkable improvement. On admission the patient weighed 134 lb., and he claimed to have lost 40 lb. in the preceding seven months. By June, 1954, his weight had risen to 150 lb., and he said he had never felt better, being totally free from dyspnœa, palpitation, and headaches, and that his sight was constantly improving. He was walking three or four miles daily. During July, 1954, he drove his car 400 miles through Canada and then returned to his former job as a weaver in a textile mill, where he tends 52 looms.

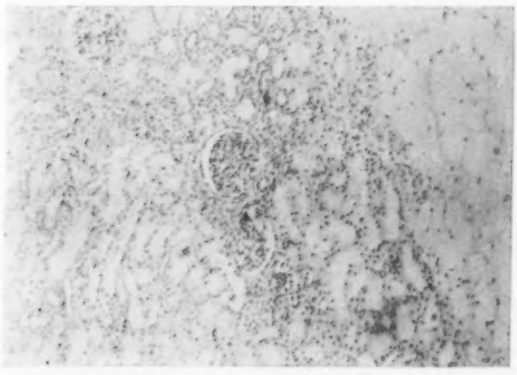

Fig. 2—Random section from kidney, showing normal structure. (Hæmatoxylin and eosin.)

Follow-up.—The patient was last studied in this hospital in December, 1957 (about four years after nephrectomy). For one and a half years after the operation he had remained in excellent general condition without medication of any kind and continued to maintain the striking improvement already described. During the past year and a half, because his systolic blood-pressure had been found at times to be 180 mm. Hg, his personal physician had treated him with hydrallazine rauwolfia ('Raudixin'). At follow-up his blood-pressure was 166/80 mm. Hg in the recumbent position and 140/70 mm. Hg when he was standing. Radiography of his chest showed the cardiac silhouette unchanged from two years ago; it remained slightly enlarged without signs of congestive failure. An electrocardiogram was also identical with that of March, 1955. His urine contained no albumin, sugar, or pathological sediment. His optic fundi were examined by the same ophthalmologist who had observed him before and after nephrectomy; no changes were found from their condition at September, 1955, and the patient's vision was O.D. 20/25, O.S. 20/30 (with glasses). The ophthalmologist's impression was grade-II hypertension, grade I/II arteriosclerosis. The patient reported "feeling better than ever," sleeping soundly, and without headaches. He walks daily about two miles without discomfort.

Discussion

Experimental Background

In their original and subsequent investigations Wilson and Byrom used the Wistar strain of rats, which were prepared by applying an annealed silver ribbon clip to one of the main renal arteries after the method of Pickering and Prinzmetal (1938). In 65% of the rats so manipulated severe hypertension was produced in 1–28 days and lasted, in some rats, nine months. The silver clip was applied so as to narrow the main renal artery without completely occluding its lumen, accomplishing the same thing technically and physiologically as the Goldblatt clamp. Daniel et al. (1954) have shown, by angiography, vasoconstriction of the intrarenal blood-vessels and parenchymal ischæmia within the "clipped" kidney in hypertensive rabbits. Wilson and Byrom found in 77% of their rats malignant nephrosclerosis in the unclipped kidney and normal histology in the protected "clipped" kidney.

Now Goldblatt, who failed to reproduce these findings in the dog and the sheep, considered that the characteristic malignant arteriolar lesions in the unclipped kidney of the rat could have been the result of pyelonephritis or of unrecognised disease in the clipped kidney. Wilson (1953) then re-examined their material by using their control rats and concluded that their original interpretation of the renal lesions was correct and that the lesions were not the result of laboratory infections. Confirmation of these unusual vascular findings by Daniel et al. (1954) suggests strongly that the rat's kidney behaves more like the human kidney than like that of the dog. Species differences are well known in laboratory investigations (Daniel et al. 1952).

Wilson (1953) next made some experiments which even more closely incriminated the kidney in hypertension. He noted that, if a rat was made hypertensive by the application of a clip to one main renal artery, excision of the contralateral unclipped kidney did not lower the blood-pressure; but, if the clip was removed to the main artery of the other kidney the blood-pressure usually dropped to normal.

The foregoing experiments were made on rats with acute hypertension but subsequent experiments on rats

with long-standing hypertension showed that, in chronic hypertension, simple removal of the clip often did not reverse the hypertension. Wilson (1953) considered that this was due to irreversible changes within the other kidney, which in time came to resemble the effect of a " clip " in producing renal ischæmia.

In further support of their theory they produced chronic hypertension by stenosis of one renal artery until the damage in the contralateral kidney was irreversible. The clip was then removed, and the hypertension persisted. Finally, the unclipped kidney with irreversible changes was removed from these rats with chronic persisting hypertension, and the blood-pressure promptly fell to normal. Such observations lend strong support to the renal genesis of this type of hypertension and of the malignant variety in particular.

Abeshouse (1941) reviewed the published cases and enumerated the underlying lesions, ranging from renal tuberculosis to renal aneurysms. However, at that time the significance of stenosis of the main renal artery as a cause of hypertension was not fully appreciated. In a complete review of the English and American published cases we have found 21 in which stenosis of the main renal artery of one kidney was considered to be the chief cause of the hypertension. All these cases have certain clinical and pathological features in common which imitate the experimental syndrome in rats. Although certain data are missing, one can justifiably presume what the completed picture would be and infer that these cases represent hypertension resulting from stenosis of a renal artery, with pathological changes reaching one of the several stages of the experimental syndrome.

In the 9 cases in which both kidneys were examined few if any pathological changes were reported in the kidney protected by the stenosis, whereas in the contralateral kidney were severe degenerative changes mainly resembling nephrosclerosis. This dissimilarity between the two kidneys is difficult to explain on a basis of chance findings. In the present case the renal histology was not remarkable in the excised kidney (which was protected by the stenosed artery in a manner comparable to the clipped kidney in the rat), but the changes in the arterioles of the ureter suggest that there may well have been vascular changes in the other kidney. In 14 of the 21 cases nephrectomy cured the hypertension. In 1 case the stenosis of the artery was alone corrected without removing the kidney, and normotension was restored. It is reasonable to suppose that some of the patients who died could have been saved by nephrectomy.

We must emphasise again that we have reviewed only those 21 cases in which a main renal artery to one kidney only was stenosed: in 1 case the stenosis was due to encroachment by a tumour; in 1 other it was caused by an aneurysm; and in the remaining 19 the artery was narrowed by an arteriosclerotic plaque (but histological proof was not always obtained). Although encephalopathy developed in 8 cases, 3 of these patients were still well at the end of two years, and in the remaining 5 cerebral changes were not mentioned, or else the disease had not progressed so far. Uræmia was an accompanying condition in only 3 of the 8 with encephalopathy. All 8 had severe hypertension, the lowest blood-pressure being 180/110 mm. Hg. These observations show how closely human material, even in limited amount, fits the criteria which appear to be important in the experimental syndrome in rats.

In looking for published cases of stenosis of a main renal artery we found 20 other cases of hypertension thought to be the result of renal ischæmia but excluded them for various reasons (Bourne 1954, Masiloff and Macht 1951, Aronson and Sampson 1951, Perera and Haelig 1952, Fishberg 1941, Wainwright 1949, Hussar and Bernstein 1954, Prinzmetal et al. 1942, Howard et al. 1954, Blahd et al. 1952, Yuile 1944, Leiter 1938, Hoffman 1942, Perry 1945).

Diagnosis

Clinicians are cautious about diagnosing hypertension due to unilateral renal disease. The treatment implies nephrectomy, and past experience has shown that only a fifth of the unselected cases of hypertension and unilateral renal disease would be helped. However, if the syndrome accurately resembles that described here, the cure-rate will be very much higher.

The ideal candidate is a patient with severe hypertension (a raised diastolic blood-pressure of 110 mm. Hg or higher) in whom the disease is rapidly progressing and more organs are becoming affected. The heart may exhibit severe electrocardiographic changes, left ventricular strain, and T-wave changes. Encephalopathy with coma, stupor, or convulsions may ensue. The signs may vary according to the duration and severity of the hypertension; but, if the changes are severe, there is all the more reason for considering the present syndrome; the severity of these changes should not contraindicate surgery. Intravenous and retrograde pyelography should aid in localising the disease, but their interpretation may be uncertain, as the 2 cases of Howard et al. (1954) showed. If there are electroencephalographic or other cerebral changes, lumbar puncture should be done to rule out arteriosclerotic encephalopathy. Pickering et al. (1952) observed that, when albuminuric retinitis is present, the pressure of the C.S.F. is nearly always above the level at which brain tumours cause papillœdema. In arteriosclerotic retinitis with encephalopathy the pressure of the C.S.F. is lower. The usual renal-function tests are not easy to assess, because apparently poor function can be reversed dramatically after nephrectomy. The regitine test is of no value, because it may be positive in the present syndrome and in the presence of uræmia, as is well known. If intravenous pyelography is not conclusive, aortography is of the greatest importance, as in the cases reported by Howard et al. (1954) and Freeman et al. (1954).

The ocular fundi should be carefully examined. The observation of Volhard and Fahr (1914) that the distinctive feature of malignant hypertension is albuminuric retinitis (hypertensive neuroretinopathy) still receives strong support. It is distinguished from arteriosclerotic retinitis by the presence of bilateral neuroretinal œdema, which is absent in arteriosclerotic retinitis except as a consequence of venous thrombosis.

Recent studies by Howard et al. (1956) indicate that there is a method of detecting the " endocrine " kidney when intravenous pyelography and/or aortography are negative: urine is collected from each kidney through retrograde catheters, and the amounts of sodium and chloride in it are measured. The endocrine or pathological kidney is detected by its decreased excretion of sodium and water.

Pathology

A study of 21 published cases selected as representing the syndrome produced experimentally in rats by Wilson and Byrom (1939) has brought forth very interesting facts. In all of them a renal artery was narrowed. Of the 11 surviving patients who underwent nephrectomy no

histological data are available about the kidney which still remains in situ, but of the excised kidneys 7 had completely normal renal parenchyma, 3 had areas of tubular atrophy, and 1 had interstitial inflammation and fibrosis. These latter abnormalities were not considered severe enough to cause the hypertension. Of the 8 patients who died 7 at necropsy had malignant nephrosclerosis of the kidney whose artery was patent and only minor or indifferent changes in the kidney protected by the stenotic artery. In Stewart's (1941) case there was parenchymal atrophy only on the side where the artery was fully patent; this case should therefore probably not be considered typical of the present syndrome, because it does not fulfil all the criteria. Blackman (1939) found at necropsy narrowing of the renal artery in 43 of 50 cases of essential hypertension but only in 5 of 50 non-hypertensives. Narrowing of the artery per se is therefore insufficient to diagnose the present syndrome; the diagnosis must rest on the complete clinicopathological picture. The 2 cases reported by Thompson and Smithwick (1952) are exceptional in that, as a result of biopsy, definite dissimilarities between the affected and the "protected" intact kidneys of surviving patients were observed: the pathological changes in the "protected" kidneys were minimal in contrast to those in the other kidneys with patent arteries. This shows the value of renal biopsy as a guide to prognosis and diagnosis.

Treatment

This syndrome has been alleviated surgically in various ways, but the series is too small for statistical analysis. Of the 21 cases 11 were cured by nephrectomy. In 1 case (Freeman et al. 1954) relief of the stenosis of the renal artery lowered the blood-pressure. In another case (Thompson and Smithwick 1952) removal of an aneurysm did not change the blood-pressure; but it is not stated whether the diameter of the artery had been changed, as was so well shown by aortography in the case of Freeman et al. (1954). Goodman (1952) reported a case in which neither medical treatment nor bilateral lumbodorsal sympathectomy altered the course of the disease, which was fatal. Thompson and Smithwick (1952) also noted failure of lumbodorsal sympathectomy to effect improvement.

The importance of the cure-rate in relation to the pathology is shown by Smith (1948) in his review of 242 nephrectomies done on patients with hypertension and various renal diseases, his cure-rate being only 19%. However, his criteria for cure were rather rigid, and we prefer a higher residual systolic level than 140/90 mm. Hg provided there is evidence of reversal of the disease in other organs, as was shown in the present case. In the 21 selected cases with renal-artery stenosis the cure-rate for such severe hypertension is remarkable and shows that satisfactory treatment and recovery are possible when the present syndrome is correctly diagnosed.

The varied effects of acute and chronic hypertension in the rat suggest the following alternatives:

(1) If the hypertension is of short duration, either nephrectomy or removal of the constricted part of the renal artery should relieve the hypertension.

(2) If the hypertension has lasted long enough, removal of the "clipped" kidney may be insufficient to relieve the hypertension, because the changes in the other kidney have become irreversible, and lumbodorsal sympathectomy also may be necessary.

The challenge to the surgeon lies in a better preoperative selection of the patients who will benefit solely by nephrectomy. The test of Howard et al. (1954) is most important in this connection.

Summary

A clinicopathological syndrome of hypertension which is cured by nephrectomy is discussed.

Wilson and Byrom had previously described this syndrome in rats.

A human case is now reported.

A review of the published cases suggests that this syndrome is less rare than is usually supposed.

Addendum

Since the preparation of this manuscript Poutasse and Dustan (1956) have described some cases of this syndrome.

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NUCLEAR CHANGES IN ORAL EPITHELIAL CELLS IN SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD DUE TO VITAMIN-B_{12} DEFICIENCY

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To make the diagnosis of subacute combined degeneration of the spinal cord due to vitamin-B_{12} deficiency is seldom difficult when there is a concomitant megaloblastic anæmia with a histamine-refractory achlorhydria. But when there are no changes in the blood and bone-marrow the clinical picture differs little from that of other diseases affecting the posterior and lateral columns. Formerly the diagnosis could be reached only *ex juvantibus*, on improvement under treatment with liver extract or vitamin B_{12}; but in recent years more certainty has been obtained by demonstrating a low serum-vitamin-B_{12} level (Mollin and Ross 1954, Victor and Lear 1956, Killander 1958, Spray and Witts 1958) or an impaired

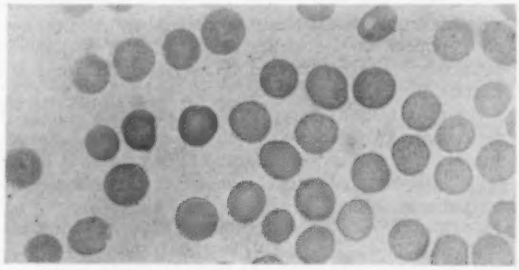

Fig. 1—Blood-picture before treatment. (×720.)

absorption test with radioactive vitamin B_{12} (Berlyne et al. 1957).

One of us described nuclear changes in oral epithelial cells in patients with pernicious anæmia (Boen 1957). In association with marked nuclear polymorphism, the presence of giant nuclei was characteristic. The nuclei were more or less round and had a finely reticulate chromatin structure. Their greatest diameter was on the average, above normal. Farrant (1958) found that both the longer and the shorter axes of the nuclei were higher in pernicious anæmia than in controls—especially the shorter. This last finding can, we think, be explained by so many of the nuclei being nearly round.

The question arose whether the nuclear changes would be found also in those rare cases in which vitamin-B_{12} deficiency is manifested by neurological disorders without hæmatological changes (Boen 1957). Recently we were able to study such a case.

Method of Investigation

The patient is asked to rinse his mouth thoroughly three times with physiological saline solution so as to remove food remnants. The mouth is then washed twice again, and the material thus obtained is centrifuged for about 10 minutes at 1000 r.p.m. The sediment is smeared evenly on microscope slides with a vaccinostyle, air-dried, and stained with May-Grünwald-Giemsa stain. A hundred consecutive nuclei are measured in their greatest diameter with an ocular micrometer using an oil-immersion objective.

Normally a maximum of 5% of the nuclei have diameters of 14·5 μ or more; in seven out of ten patients with pernicious anæmia the nuclei were definitely abnormal; in these seven cases we found the large nuclei in an average of 26%.

Case-report

Miss A, aged 57, had worked as a charwoman for the past six years without any long absences through illness. In July, 1957, she noticed tingling at the volar side of the fingers, but it did not interfere with her work. In October she complained of increasing general weakness, and had to take to her bed.

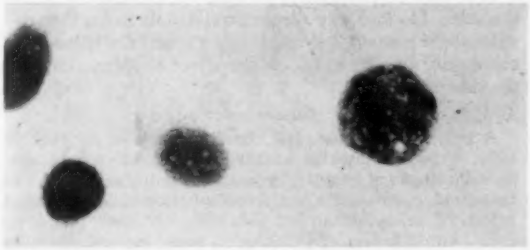

Fig. 2—Mouth-washing before treatment. Giant nucleus beside normal ones. (×900.)

She had uncontrolled jerks of the legs, paræsthesiæ, and numbness of the feet, and could barely walk from bed to table. In December she was admitted to the Burgerziekenhuis.

Examination showed no anæmia, icterus, or œdema; the liver and spleen were not enlarged. There was no glossitis, and the tongue was normally papillated except at the edges. Dr. S. Waterman, neurologist, found hypotonia and paresis in both legs (affecting the proximal part more than the distal), hyperactive patellar and Achilles reflexes, and slight ataxia. Somewhat later Dr. P. L. Braat, neurologist, also found impaired vibration sense in both legs and loss of position sense in the toes. There were bilateral extensor plantar responses, positive Chaddock and Mendel-Bechterew reflexes, and on the left side knee clonus. The cerebrospinal fluid was normal in pressure, clear, and colourless, and contained no granulocytes: the Wassermann, Pandy, and Nonne reactions were all negative.

Hæmoglobin 14 g. per 100 ml. Sedimentation-rate (Westergren) 7 mm. in one hour. Serum not icteric. Leucocytes 7800 per c.mm. (eosinophils 1%, granulocytes 69%, lymphocytes 24%, monocytes 6%). No hypersegmentation of granulocytes. Erythrocytes normal (except for slight anisocytosis); no megalocytes (fig. 1). Number of platelets normal. Bone-marrow picture entirely normal; no megaloblasts or giant metamyelocytes. Reticulocyte-count 1·5%. Serum-iron concentration 140 γ per 100 ml. (normal).

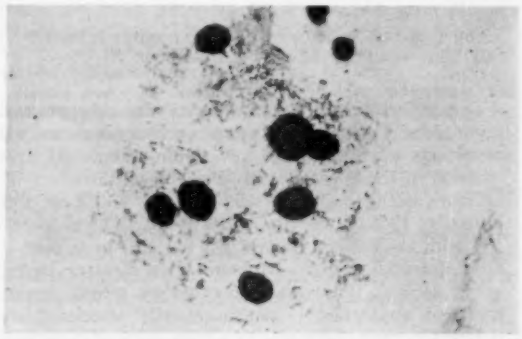

Fig. 3—Mouth-washing before treatment. Polymorphism of nuclei. Typical of vitamin-B_{12} deficiency. (×400.)

Gastric analysis showed histamine-refractory achlorhydria. The luetic serological reactions were negative. The urine, with a specific gravity of 1·029, contained no urobilin.

In contrast to the hæmopoietic system the oral epithelial cells were distinctly abnormal. There was pronounced polymorphism of the nuclei and there were characteristic giant nuclei, more or less round and with a finely reticulate chromatin structure (fig. 2). 19% of the nuclei had a diameter of at least 14·5 μ, compared with 5% or less in normal people (fig. 3).

A diagnosis of vitamin-B_{12} deficiency was made on these changes in the epithelial cells of the mouth, and the patient was treated with 100 γ vitamin B_{12} by intramuscular injection daily for 3 weeks, and thereafter once a week. Her legs gradually grew stronger and after a month she could walk short distances without support. The paræsthesiæ, the numbness, and the abnormal reflexes disappeared. The slight ataxia and the impairment of vibration sense remained.

The administration of vitamin B_{12} had no influence on the reticulocyte-counts, the hæmoglobin concentration, or the serum-iron level. These prove that the hæmopoietic system had not suffered from the deficiency.

The oral epithelial cells were normal again a week after the beginning of treatment. Fig. 4 shows the distribution of the nuclei on different days: by the 5th day large nuclei had disappeared. This reaction to vitamin B_{12} is similar to that of patients with classical pernicious anæmia (Boen 1957). In fig. 5 the more monomorphic picture of the nuclei can be seen.

Another proof of the correctness of the diagnosis was the low serum-vitamin-B_{12} level before treatment—namely, 60 $\mu\mu$g.

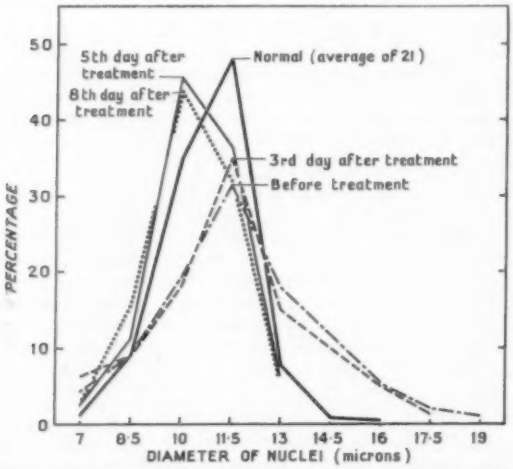

Fig. 4—Distribution of nuclei on different days after beginning treatment with vitamin B_{12}.

per ml. (normal 150–500 $\mu\mu$g.).* The outcome was known to us only later, when the patient was recovering.

Discussion

It is generally agreed that patients with subacute combined degeneration of the spinal cord concomitant with pernicious anæmia have a low serum-vitamin-B_{12} level, whereas in those with other neurological disorders it is normal (Mollin and Ross 1954, Victor and Lear 1956, Killander 1958, Spray and Witts 1958). The absorption test with radioactive vitamin B_{12} has also been used for the differential diagnosis of neurological diseases (Berlyne et al. 1957). This test is not always useful, because impaired absorption is not necessarily associated with deficiency, since there may be a large stock of vitamin B_{12} in the body. Again, though absorption is normal, there may be deficiency because the diet, over a long period, contains too little vitamin B_{12}, as in some vegetarians.

* The assay was done in the microbiological department of Organon-Oss, using *Lactobacillus leichmannii*.

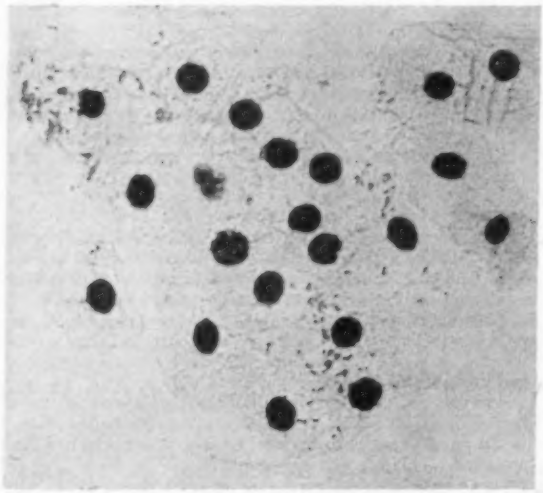

Fig. 5—Mouth-washing on 8th day of treatment. Normal picture. (×400.)

(Badenoch 1956, Booth and Mollin 1957). The characteristic changes in the nuclei of the oral epithelium, however, appear to be definite evidence of vitamin-B_{12} deficiency. Their detection is easy and the method is suitable for clinical purposes.

A normal nuclear pattern does not exclude a vitamin-B_{12} deficiency. In three out of ten patients with pernicious anæmia the nuclei were normal (Boen 1957). Farrant (1958) also found a normal average diameter in some of his patients.

Summary

A woman, aged 57, had had subacute combined degeneration of the spinal cord for several months, but showed no changes in the blood or bone-marrow. The diagnosis of vitamin-B_{12} deficiency was made on characteristic nuclear changes in the oral epithelium. On treatment with vitamin B_{12} she much improved and the nuclei of the oral epithelium became normal within a week of the start of treatment. No changes were seen in the hæmoglobin concentration, reticulocyte-counts, or serum-iron level. The diagnosis was confirmed by demonstration of a low serum-vitamin-B_{12} level before treatment (60 $\mu\mu$g. per ml.).

We are grateful to Prof. J. G. G. Borst for his encouragement, to Mrs. J. M. den Ottolander-Claremont for correcting our English, and to Organon-Oss for estimating the serum-vitamin-B_{12} level.

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SARCOIDOSIS OF LIVER AND SPLEEN

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SARCOIDOSIS is now being diagnosed more often than formerly. Its ætiology is still a subject of controversy. Whereas many physicians regard sarcoidosis as an unusual response to tuberculous infection, others regard it as a reaction to various exciting causes.

Sarcoidosis may affect the skin lymph-nodes, the eyes, the salivary glands, the lungs, the bones of the hands and feet, the liver, and the spleen. The Mantoux reaction is often negative but may be positive, and then usually only weakly so. The lesions are granulomatous and resemble tubercles; but caseation is absent, and tubercle bacilli are never found.

The case reported here is unusual for three reasons: the sarcoid lesions were demonstrable only in the liver and spleen; the patient was aged only 13; and the spleen ruptured, enabling us to follow the effect of splenectomy on the disease.

Case-report

A boy, aged 13, attended Harefield Hospital on July 29, 1956, with two months' history of being off colour, with periodic attacks of epigastric pain and vomiting associated with rigors and anorexia. He had possibly been jaundiced a month before. Recently he had had pain in the left lower part of his chest, with a feeling of tightness on breathing and coughing. There was nothing relevant in his past or his family history.

Nine siblings had been free from similar illness.

On admission to hospital on July 29, 1956, the patient looked pale and ill but was not jaundiced. His temperature was 99°F and pulse-rate 76. The only abnormal physical signs were some impairment of percussion note, weak breath sounds at the left base, and a liver that was just palpable.

Investigations.—Radiography of his chest showed opacity at the left base but no abnormal hilar shadows. Bronchography showed a normal bronchial tree. The Mantoux reaction was positive at 1/100, but the reaction was not brisk. Acid-fast bacilli were not seen or cultured in thirteen specimens of sputum. The urine contained no bile or urobilinogen. The erythrocyte-sedimentation rate (E.S.R.) was 20 mm. at the end of one hour (Westergren), and the white blood-cells numbered 7500 per c.mm.

Progress.—For two weeks the patient's evening temperature was 99°F (see figure). The E.S.R. was 8 mm. at the end of one hour at the end of this time. 'Distaquain', penicillin 300,000 units was then given for eight days, during which time his evening temperature fell to 98·4°F; but it rose to 99·8°F when the penicillin was withheld and fell to 98·4°F when the penicillin was resumed. Then the boy was allowed home for a weekend. On his return he said that on the previous evening he had had abdominal pain and a headache and had vomited. He felt better on return but looked ill and tired, and his temperature had risen to 100°F. Jaundice was absent, and no lymph-nodes were palpable. His spleen had become palpable and his liver larger. The Paul-Bunnell reaction was negative, a blood-culture was sterile, the Wassermann reaction and the Kahn test were negative, and acid-fast bacilli were not found either on direct examination or on culture on numerous occasions throughout his illness. Reticulocytes were less than 1%, and sternal marrow showed a maturation defect of red and white series. Liver-function tests showed alkaline phosphatase 8 King-Armstrong units; bilirubin 0·2 mg. per 100 ml.; thymol turbidity 1 unit; no flocculation; total protein 7·12 g. per 100 ml. (albumin 5·25 g. per 100 ml., and globulin 1·87 g. per 100 ml.). The liver and spleen continued to increase in size, and the temperature swung between 100° and 104°F. Penicillin appeared to lower the temperature to 99°F in the evenings. There was still no other abnormality, so on Sept. 14, 1956, the abdomen was opened.

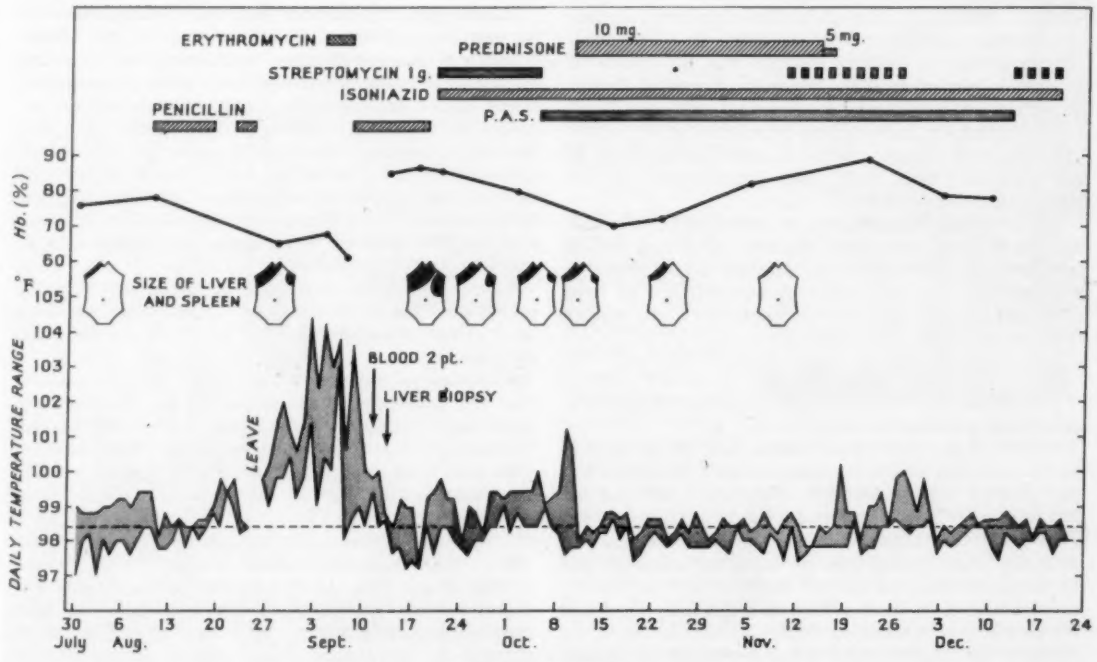
On laparotomy the liver was found to be enlarged and looked normal but was rather firm. The spleen was smooth and much enlarged. No other abnormality was found in the abdomen. A biopsy specimen taken from the liver showed scattered aggregations of epithelioid cells, some with giant cells; there was no caseation, and tubercle bacilli were not seen. Sarcoidosis was diagnosed.

Postoperative course.—This was uneventful, and treatment with isoniazid and streptomycin was started. Because of hypersensitivity p- aminosalicylic acid was later substituted for the streptomycin. The liver became a little smaller, but the boy was still pyrexial and miserable. Treatment with prednisone produced a dramatic response: the boy looked better, his pyrexia fell by crisis, and in forty-eight hours his liver was much smaller and his spleen impalpable. His liver continued to decrease, and the drugs were stopped. He had slight pyrexia for a fortnight after the prednisone had been stopped, but thereafter his temperature was normal.

On discharge in March, 1957, he was apyrexial and had put on weight, and neither liver nor spleen were palpable. The E.S.R. was 20 mm. at the end of one hour (Westergren). During all this time he had remained anæmic. At the onset his hæmoglobin was 68%, white-cells 3500 per c.mm., and platelets 100,000 per c.mm. This condition was unaffected by chemotherapy and parenteral iron. Prednisone, however, caused the hæmoglobin to increase by 20%.

Readmission.—In August, 1957, because of pyrexia and occasional nausea and vomiting the patient was reinvestigated. During ten days in hospital he had no pyrexia and no abnormal physical signs. Liver-function tests were normal; agglutination reactions against salmonella and brucella were negative, the hæmoglobin was 80%, and the E.S.R. was 20 mm. at the end of one hour (Westergren).

Rupture of spleen.—On Sept. 6, 1957, the boy was thrown off his bicycle, striking his left side on the handlebars. He was admitted to Mount Vernon Hospital half an hour later. He complained of severe upper abdominal pain, mainly on the left side.



Treatment and progress.

On examination he was vomiting and presented the signs of acute hæmorrhage; his abdomen was tender all over but maximally in the left hypochondrium, where guarding was present. His abdomen was slightly distended, and shifting dullness was present on the right side. Shoulder pain was absent.

At laparotomy by Mr. Alan Shorter two hours later, his abdomen was found to contain a pint and a half of blood, and there was a tear at the hilum of the enlarged spleen. Splenectomy was done and three pints of blood transfused. Convalescence was uneventful, and the boy was discharged on the eleventh postoperative day with hæmoglobin 74%.

Operation specimen.—The excised spleen weighed 370 g. (normal for age, 100 g.) and had a transverse tear extending from the hilum for 5 cm. Its capsule was smooth and covered with blood-clot. On section a central band of hæmorrhage at the site of the tear was seen, flanked by pale splenic substance showing fine white mottling. Microscopy showed an area of interstitial hæmorrhage surrounding the tear and the typical appearances of active sarcoidosis in the splenic substance (small aggregations of epithelioid cells, some with giant cells, surrounded by a thin zone of lymphocytes, but no caseation).

Follow-up.—Seen on Dec. 13, 1957, three months after the operation, the boy was in excellent clinical condition. His liver was impalpable, his hæmoglobin 92%; E.S.R. 8 mm. at the end of one hour (Westergren), white cells 12,100 per c.mm. (polymorphs 45%, lymphocytes 46%, eosinophils 6%, basophils 2%, monocytes 1%).

Comments

In this case the presenting symptoms of pyrexia and malaise were probably due to the sarcoid lesion. The cough and tight feeling in the left side of the chest may have been due to the slight changes in the left base but were more probably due to irritation of the diaphragm by an enlarging spleen.

Antituberculous drugs were without much effect, but prednisone appeared to suppress the disease. That it was only suppression was realised ten months later, when section of the spleen showed active sarcoid. The figure shows the increase of hæmoglobin associated with prednisone therapy and the relapse following its withdrawal. The recurrence of anæmia suggests that the course of prednisone was inadequate. Since the depressed hæmopoiesis caused few symptoms, surgery was not considered, but it became compulsory later by rupture of the spleen and then produced an increase of hæmoglobin, a rise in the white-cell count, and much improvement in the patient's general condition.

We have watched this case for eighteen months and have at no time found any evidence of sarcoid lesions elsewhere. The initial lesion in the chest did not resemble pulmonary sarcoid. This is very unusual, and we have only been able to find one definite case with similar features published (Kay 1950).

Discussion

Sarcoidosis may be generalised or may appear in well-recognised groups of tissue.

Mather et al. (1955) have shown that, in all types of sarcoidosis, liver biopsy is positive in 63% of patients and the spleen is palpable in 14%. Necropsy results put the incidence of splenic involvement at 50% (Branson and Park 1954); this is likely to be due to the impossibility of detecting slight enlargement of the spleen clinically and to the infrequency of splenic biopsy. In this country involvement of the liver and spleen is generally silent and the patient is only conscious of the disease elsewhere. In America cases of gross involvement of the liver and spleen, with symptoms of liver failure, have been described, but most of these are associated with manifestations elsewhere.

Liver in Sarcoidosis

Although the liver is so often involved and enlarged in sarcoidosis, evidence of disordered function is uncommon in this country. In the series of Mather et al. (1955) only 10% of the cases showed a raised serum-globulin level, and the finding bore no relationship to the presence or the absence of sarcoid lesions in the liver. In the present case liver function was normal throughout.

Jaundice is rare; Branson and Park (1954) found only 3 certain cases in 867 cases of sarcoidosis.

Liver failure can occur in sarcoidosis; Branson and Park (1954) describe a fatal case in which jaundice, ascites, and hæmorrhage occurred.

Kelley and McHardy (1955) report a man, aged 48, who developed obstructive jaundice due to hepatic sarcoid lesions. The liver became fibrotic, and he died in liver failure. He was treated with corticotrophin and deep X rays; the latter may have been a major factor in producing the cirrhosis.

In these cases hepatic involvement was only part of a generalised sarcoidosis.

Spleen in Sarcoidosis

Involvement of the spleen in the present case produced hypersplenic anæmia and was a contributory factor in rupture of the spleen.

Hæmopoietic dysfunction is not uncommon in sarcoidosis. Hypersplenism may depress the red cells, white cells, or platelets, either severally or together. In the present case the red-cell count was chiefly affected, and the white-cell count during hyperpyrexia fell to 3500 per c.mm., and for three months (from September to November, 1956) the platelet-count was 100,000–150,000 per c.mm. There were no purpuric manifestations. Bruschi and Howe (1950) described a case in which splenectomy had to be done to relieve purpura.

It is thought that the anæmia is due to exaggeration of the normal inhibition of the bone-marrow by the spleen. Whether prednisone increased the hæmoglobin by acting directly on the marrow or by decreasing the volume of the spleen and the sarcoid lesions contained therein is questionable. Shulman et al. (1952) noted, in a series of cases, that corticotrophin caused rapid regression of hepatosplenomegaly, with occasional improvement of anæmia, but in most cases relapse followed the withdrawal of corticotrophin. The similar effect produced by splenectomy has been recorded by Longcope and Freiman (1952) and Kay (1950).

Nausea, vomiting, and pain in the chest were all probably related to splenomegaly. Splenectomy was done by Partenheimer and Meredith (1950) to relieve these symptoms.

Spontaneous rupture of the spleen from sarcoidosis was the presenting symptom in a case described by James and Wilson (1946) and another by Phillips and Luchette (1952). The former patient was a man, aged 49, who had pulmonary lymphadenopathy and a normal-sized spleen; the diagnosis was made on finding sarcoid lesions in the spleen. The latter patient was a man, aged 21, who had lymphadenopathy and a spleen weighing 306 g. Neither of these patients had isolated sarcoidosis of liver or of spleen. In the present case the rupture was traumatic, but probably the trauma would not have ruptured a normal spleen. This accident enabled us to observe the persistence of the sarcoid lesions despite antituberculous chemotherapy and a short course of

prednisone. It also suggests that splenectomy would have controlled the anæmia had it been done before the rupture.

Summary

A case of sarcoidosis of the liver and spleen is described in a boy, aged 13, complicated by hypersplenism and traumatic rupture of the spleen.

We wish to thank Dr. E. Idris Jones, consultant physician, who originally referred the patient; Mr. David Levi, consultant surgeon, for the liver biopsy; Dr. E. Nassau, pathologist and his staff for the histology of the liver biopsy; and Dr. G. S. W. Andrews and Dr. J. M. Bennett, pathologists, of Mount Vernon Hospital, for the report on the spleen, and Mr. A. Shorter, consultant surgeon, for the splenectomy.

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DISSEMINATION OF MICRO-ORGANISMS BY A SURGICAL PUMP

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IN a case of staphylococcal subphrenic abscess treated by suction drainage by an electric pump it was noted that the outlet from the pump discharged directly into the ward. When the air from the outlet of the pump was led to a slit sampler, it was found that large numbers of organisms were being ejected by this route.

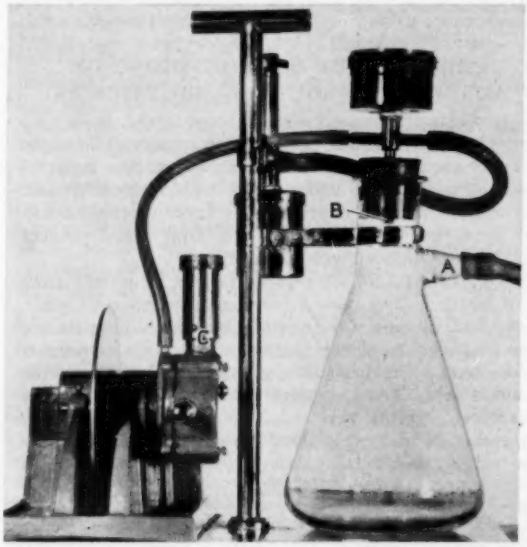

Fig. 1—The pump assembly: A, input to trap; B, outlet from trap to pump; C, outlet from pump (as modified).

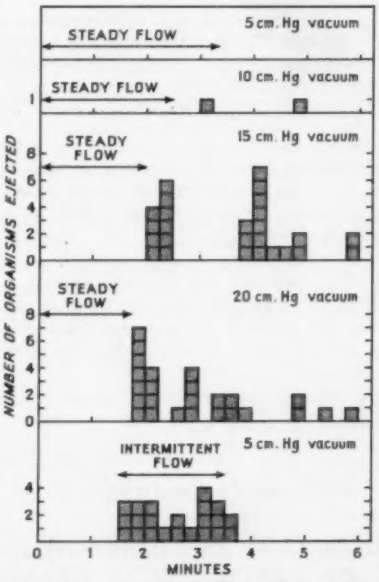

Fig. 2—Numbers of organisms ejected from pump outlet at different pressures and flows.

Since the discharge of organisms in this way into a surgical ward was clearly undesirable, experiments were instituted to show the degree of contamination of the atmosphere in this way and to find a way to prevent it.

Degree of Contamination

The input to the trap (fig. 1, A) was immersed in 200 ml. of broth culture containing 100,000,000 organisms per ml., and the outlet from the pump (fig. 1, C) was led by a sterile plastic tube to a slit sampler. The pump was run at negative pressures of 5, 10, 15 and 20 cm. Hg.

Fig. 3—Filter assembly showing brass cylinder, mesh cap, and cotton-wool.

Fig. 2 shows representative examples of the results obtained. With a vacuum of 5 cm. Hg no organisms were ejected. With the greater negative pressures used no organisms were ejected during the flow of the liquid, but a shower of organisms was ejected when the container emptied and air and froth were drawn rapidly into the trap (fig. 2). The number of organisms ejected increased with increase of the vacuum, and this was partly because bubbles in the trap came into direct contact with the tube (fig. 1, B) leading to the pump.

In view of the importance of splashing and the likelihood of this occurring in practice when the drained cavity empties, experiments were conducted in which the

200 ml. of culture was delivered at intervals by a siphon in 20-ml. amounts. In this way repeated splashing and frothing occurred. In these circumstances 5–10 times as many organisms were ejected as when the same volume was delivered by direct flow (fig. 2).

Prevention

Ejection of organisms from this system was completely abolished by fitting to the output of the pump a brass sleeve, with a mesh floor and cap, lightly packed with non-absorbent cotton-wool (fig. 3). This filter has remained effective during 24-hour periods of continuous running of a modified experimental system in which 20 ml. amounts of culture were delivered at intervals of 2 minutes. In practice the non-absorbent cotton-wool has been replaced every 24 hours when the pump was in continuous use.

The brass sleeve was made by Mr. D. Brown, of the electrical engineer's department, Middlesex Hospital, and costs about 7*s*. 6*d*.

Preliminary Communications

INCORPORATION OF CARBOXYL-CARBON ATOM OF GLYCINE INTO OXALATE IN A CASE OF PRIMARY HYPEROXALURIA

PRIMARY hyperoxaluria [1] is characterised biochemically by a continuous urinary oxalate excretion equivalent to about 100–200 mg. $(COOH)_2 . 2H_20$ per 24 hours. (The corresponding figure for normal people is less than about 40 mg.). Clinically, these patients present in childhood with recurrent multiple calcium-oxalate urinary calculi and nephrocalcinosis; they die prematurely from renal failure, and at necropsy calcium oxalate crystals are demonstrable in some of the extrarenal tissues.[2] Previous studies in this laboratory suggested that glycine is the precursor of at least some of the oxalate which they excrete.[3]

We recently administered glycine–1–^{13}C orally (2·56 mg. per kg. body-weight, 49·8 atoms % ^{13}C excess, 6-hourly for 4 days) to a patient with primary hyperoxaluria; the oxalate was isolated from successive 6-hour urine collections and its ^{13}C content measured. There was prompt and considerable incorporation of the isotope into the urinary oxalate (see figure). This relation between glycine and oxalate in primary hyperoxaluria accords with our previous observation that in this disease large doses of sodium benzoate (given to deplete the free-glycine metabolic pool) decrease the urinary excretion of oxalate.[3]

It has been shown that enzyme systems capable of degrading glycine via glyoxylate to formate and carbon dioxide are present in some mammalian tissues [4]; also (during in-vitro experiments with rat liver) that, if the degradation of glyoxylate to formate and carbon dioxide becomes the rate-limiting step in the reaction sequence, oxalate is synthesised.[5] Although our present findings are compatible with the view that the metabolic lesion of primary hyperoxaluria is in this path of glycine metabolism, they do not show whether the primary abnormality is (a) a failure to degrade glyoxylate to formate and carbon dioxide, or (b) an excessive—possibly abnormal—conversion of glycine to glyoxylate, the further metabolism of which is inherently limited.

Other cases of primary hyperoxaluria are being studied, and we are comparing the isotope enrichment in the free urinary glycine (which we regard as a valid sample of the free-glycine metabolic pool [6]) with the isotope enrichment in the urinary oxalate. The results of these investigations will be reported in detail elsewhere.

We are indebted to Prof. A. Wormall, F.R.S., for facilities for the mass spectrometric analyses, and to our assistants Miss E. D. Bell and Mr. L. Rawlings for their help.

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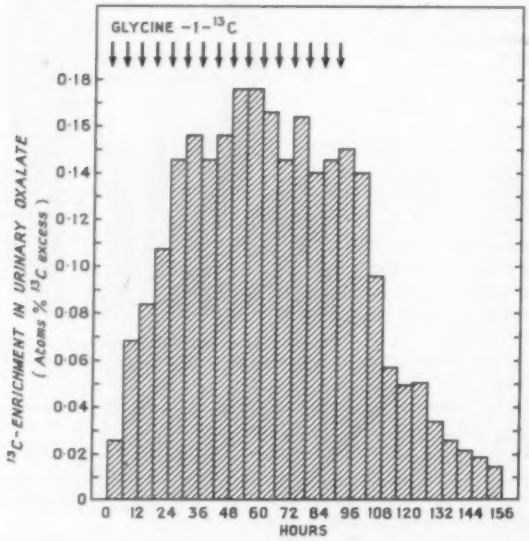

The ^{13}C abundance in the calcium oxalate isolated from successive 6-hour urine collections in a case of primary hyperoxaluria given glycine-1-^{13}C orally at the times indicated by arrows.

INHIBITION BY HYDROXYDIONE OF ADRENALINE-INDUCED ARRHYTHMIAS

DURING animal experiments, one of us (N. R. W. T.) noted that hydroxydione (21-hydroxypregnane-3, 20-dione sodium succinate) appeared to arrest cardiac arrhythmias in the isolated rabbit heart and to prevent their occurrence in cats. A preliminary series of experiments has now been done to see if this drug would prevent arrhythmias induced with adrenaline.

Five healthy cats were used, varying in weight from 2 to 3·5 kg. They were lightly anæsthetised with ether, a tracheal cannula was inserted, and the blood-pressure was recorded from the carotid artery with a mercury manometer. The drugs were given intravenously into the femoral vein. The vagi were left intact, and continuous electrocardiograms were recorded using lead aVF as a control. Gradually increasing doses of adrenaline, within the range 100–500 μg., were given intravenously and a

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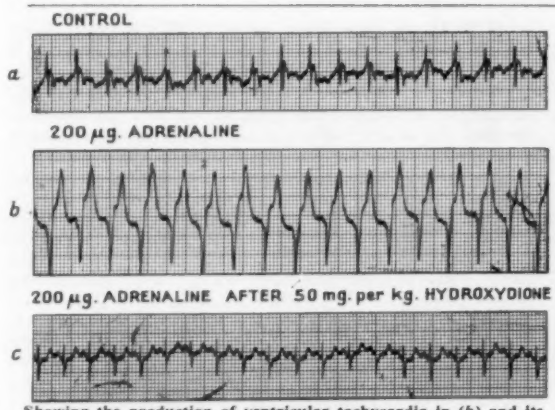

Showing the production of ventricular tachycardia in (*b*) and its prevention by hydroxydione in (*c*).

great variety of arrhythmias were induced—ectopic beats from multiple foci, coupled rhythm, nodal rhythm, and paroxysmal tachycardias. The dose, which varied greatly from cat to cat, was stepped up in each case until paroxysmal ventricular tachycardia could be consistently produced. 50 mg. of hydroxydione per kg. body-weight was then given intravenously, and after 6 minutes the previously determined dose of adrenaline was repeated. In four out of five cats none of the previously recorded arrhythmias occurred (see figure), and after 50 to 100 mg. hydroxydione per kg. body-weight the dose of adrenaline had to be increased by 50–300% before the tachycardia was reproduced.

It may be that hydroxydione or one of its congeners could prevent arrhythmias induced in other ways, and might be useful as an anæsthetic agent during cardiac surgery. These possibilities are under study.

We are indebted to Messrs. Organon Laboratories for a supply of hydroxydione.

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Reviews of Books

Clinical Electrocardiography

The Spatial Vector Approach. ROBERT P. GRANT, M.D., National Heart Institute, National Institutes of Health, Bethesda, Maryland. London and New York: McGraw-Hill. 1958. Pp. 225. 58*s.* 6*d.*

THIS outstanding book on clinical electrocardiography is based on a study of the direction of spread of the electrical forces of the heart as shown by the spatial vector. It is Dr. Grant's opinion that no loops need be actually calculated and no special apparatus is required. He emphasises that the direction of the loop can be appreciated with sufficient accuracy by simply studying the standard limb and chest leads of the electrocardiogram.

The electrocardiogram is a graphic record of the electrical impulses which spread from the sino-atrial node across the atria to the atrioventricular node and then via the bundle of His to the ventricles. These electrical forces are transmitted to the surface of the body and may be tapped at different points by leads attached to the limbs or chest wall—the electrocardiogram. The form of the electrocardiogram in any one lead was once thought to reflect action potentials underlying the electrode, but it is now appreciated that it is merely tapping at one point the circuit of electrical forces which is described as the spatial vector or loop. Thus, the electrocardiogram represents the total electric forces at the point on the limbs or chest wall from which the lead is taken, and is as much influenced by abnormalities of ventricular muscle on the opposite side of the heart as it is by abnormalities beneath the electrode. The negative wave or Q wave of anterior chest leads in anterior cardiac infarctions, therefore, merely represents a retreat of the electrical forces posteriorly, away from the damaged area, and is accompanied by an increase in height of the R wave in posterior leads. Conversely, in posterior cardiac infarction an increase in height of the R in anterior chest leads is just as important as the presence of a Q wave posteriorly.

This is the vectorial approach and Dr. Grant uses it to explain the whole of electrocardiography. If this concept can be understood the laborious memorisation of electrocardiographic patterns becomes unnecessary. Dr. Grant's book should be read and re-read by every cardiologist or anyone training in cardiology. The reader is not presented with a series of loops divorced from electrocardiograms, but is shown how to deduce the pattern of this loop from the routine electrocardiogram. Knowledge of the approximate pattern of the loops greatly helps in basic interpretation, but the finer points for diagnosis are still obtained from changes in the form of the QRST complex picked up in individual leads. The vector approach however, gives a broad view of the whole picture and is valuable for *understanding* abnormalities shown in the electrocardiogram.

Although this is a book of first principles it is not a suitable book for the beginner, or for the occasional electrocardiographer, who will have to await a simpler volume, but preferably one based on the same principles.

Law and Ethics for Doctors

STEPHEN J. HADFIELD, M.B., D.OBST., assistant secretary, British Medical Association. London: Eyre & Spottiswoode. 1958. Pp. 388. 42*s.*

IN the hundred years since the first Medical Act of 1858, few of the changes in the practice of medicine have made its conduct simpler; for increasing specialisation, the influence of the State, and the criticism of a more educated public have brought appreciable complications. During the century, however, the profession has tested the principles of conduct which were its inheritance, and proved their fundamental strength. These have remained constant while practice has altered, keeping in step with the community's needs.

In this book Dr. Hadfield has described the many points at which medicine makes contact with the community. With so much ground to cover, some lack of detail or significant omissions might be pardoned; in fact, the book is outstandingly comprehensive; and even where complicated legal principles are being explained, the information is clearly presented. Whether describing the ethical position of a doctor who broadcasts, the legal procedure of the Coroner's Court, or prescribing in the National Health Service, Dr. Hadfield is readable and interesting.

It is possible to practise for years, maybe a lifetime, without direct knowledge of the workings of courts of law; and of the many committees and tribunals which now exist under the National Health Service. Many doctors have a vague impression of their existence and function somewhere in the professional background. This book will give them a clearer picture. To some extent it is also a catalogue of present-day medical thought and custom, and as such it is a historical document. Moreover it is a source-book for the teacher of the undergraduate and the new entrant to practice, and a work of reference for the established practitioner.

Does the place of the doctor in relation to the community, as here described, receive sufficient attention in the formal

teaching of the medical student? There is much to be said for encouraging the student to make himself more fully aware of his future responsibilities towards his patients, his profession—and himself.

Modern Trends in Endocrinology

Editor: H. GARDINER-HILL, M.D., F.R.C.P., consulting physician, St. Thomas's Hospital, London. London: Butterworth. 1958. pp. 311. 65s.

THE important Modern Trends series enables the clinician or the investigator to keep an eye on the growing points of knowledge that fall outside his own immediate interests. Some sixteen subjects have now been covered, some of them by two or even three volumes, and this one is a notable addition. It comprises 21 articles, about half of them devoted to the thyroid or the adrenal cortex. The range is wide, and includes hormones of the adrenal medulla, serotonin, and gynæcological endocrinology. The authors include physiologists, clinical investigators, and clinicians, and there is a pleasing variety about the style and approach of the different essays.

Everyone, whether primarily an investigator or a clinician, will find something to his taste; and the postgraduate student will probably want to read the whole book. But some readers will regret that in a book designed not only to satisfy curiosity but also to awaken interest the bibliographies do not include the titles of articles cited. It is admittedly hard to persuade some authors to provide them; but the practice encourages the novice to explore his medical library, and saves the investigator some unnecessary excursions into it.

Bridging the Gap

Editor: R. F. TREDGOLD, M.D., D.P.M., physician-in-charge, department of psychological medicine, University College Hospital, London. London: Christopher Johnson. 1958. Pp. 270. 30s.

MORBID public fascination by mental illness is well enough known and its dynamic origins are easy to understand: not for nothing are new psychiatric works obligatory reading for Hollywood producers. All too often what is written for the public is sensational, with grotesque distortions or malicious half-truths, and a book, therefore, which turns its back on Ruthless Exposures, and seeks rather to conciliate and explain, is to be welcomed. Here a group of experts have written for the inquiring layman upon some aspects of the mental health services, and their sober reflections are placed alongside bitter and trenchant criticisms from ex-patients and others. Emphasis is rightly placed on the harm done by mutual slanging matches between extremes of either side, and the need to travel the much harder road of reconstruction and improvement. But this book is no act of whitewash: Dr. Donald Johnson, M.P., hits out in one chapter with his customary vigour, and Dr. J. A. R. Bickford makes a splendid contribution on the psychiatrist's shortcomings and opportunities (his views should be obligatory reading for those in mental-hospital practice). Dr. J. A. Scott has several chapters on the part played by the local authority, and, among others, Dr. Desmond O'Neill writes on domiciliaries, Dr. E. W. Dunkley on the observation ward, and Dr. David Stafford-Clark on the psychopath. There is an excellent brief account of the mental defective and a useful appendix summarising the laws related to mental hospital admission.

It is perhaps inevitable that sensible balanced views should be slightly dull, but even allowing for this the book may disappoint some readers, perhaps because of the lack of continuity and repetitiveness. But we hope it will reach the very wide public which it undoubtedly deserves.

Marriage Counselling

J. H. WALLIS, training officer, National Marriage Guidance Council; H. S. BOOKER, senior lecturer in statistics, London University. London: Routledge & Kegan Paul. 1958. Pp. 313. 25s.

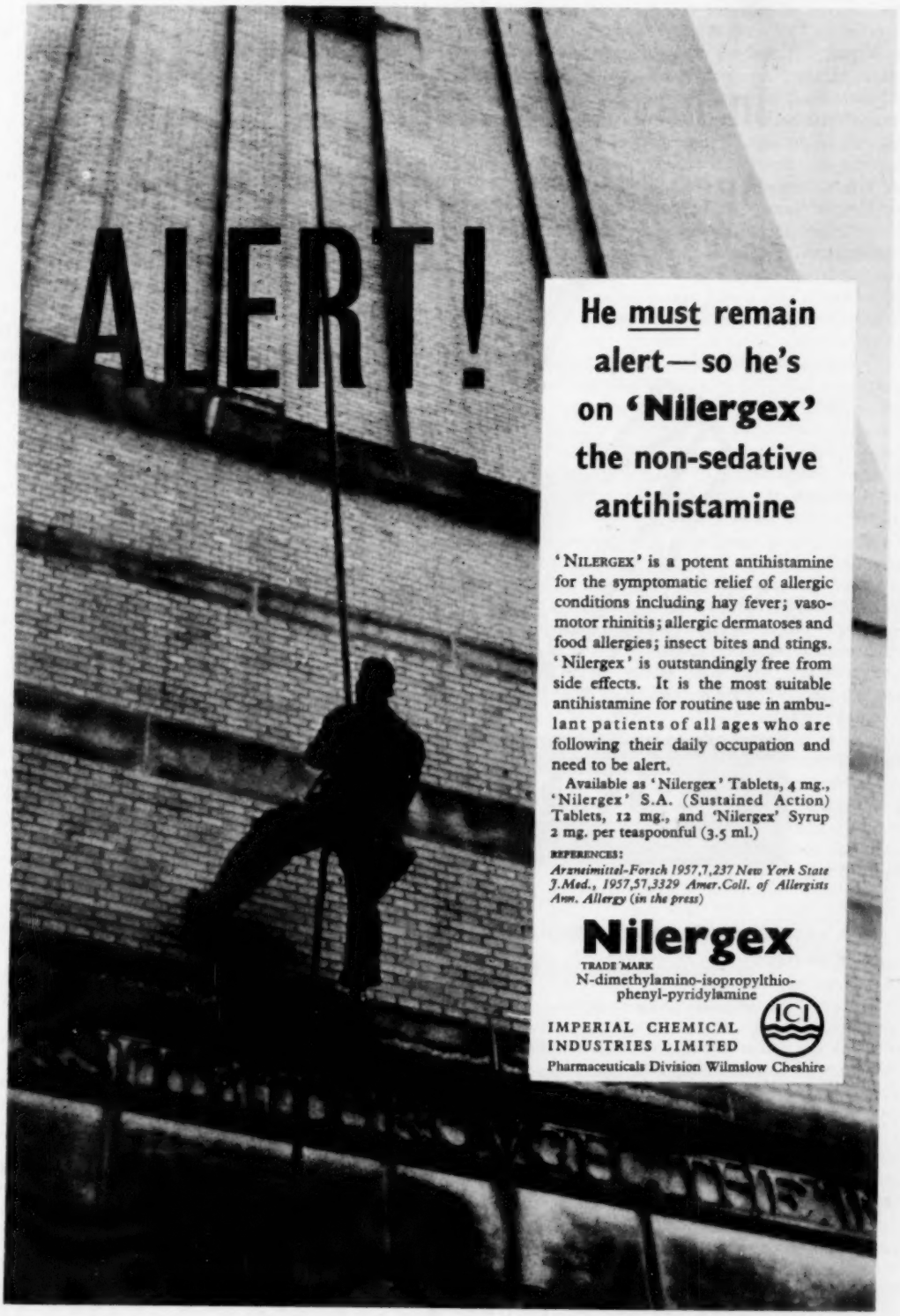
THIS is an account by Mr. Wallis of the origin, development, principles, and aims of the Marriage Guidance Council; the kind of problems brought by spouses in trouble; the methods of choosing and training counsellors (in detail) and (in less detail) the way they set about their work; followed by a statistical analysis by Mr. Booker of some 25,000 "cases" recorded by counsellors in the years 1952–54, directed mainly to ætiology.

Probably all family doctors over 40 and many other kinds of medical men or women have found themselves either essaying or resolutely declining the task of "marriage counselling". Of those not declining, probably only the few with psychiatric leanings and training—perhaps not even all these—will approach it without reluctance and misgiving. It is surprising, then, that there is apparently no lack of volunteers ready to face a residential selection conference, based on the procedure of the War Office Selection Board, for the privilege of listening to and trying to help marriage partners in distress as "counsellors", part-time and unpaid. No very clear picture emerges of the typical counsellor—if such a thing exists—either before or after training, and we do not know, for instance, whether a troubled spouse may expect to meet a counsellor of similar or dissimilar social or cultural class. The chapters on the nature of counselling and people in difficulties are modestly and pleasantly written, but their matter is sadly familiar to the medical man and the results of statistical analysis seem also to confirm everyday experience. Causes of trouble are multiple and complex—personality counts for more than environment, sexual difficulties are less intractable than those of character—and the broad results of "counselling" (a third helped, a third not helped, a third "result unknown") seem to justify the practitioner's misgiving when the history and symptoms of a sick marriage are laid before him.

Cunningham's Manual of Practical Anatomy (12th ed. Vol. III, Head and Neck: Brain. London: Oxford University Press. 1958. Pp. 520. 28s.).—The main changes in this new edition, revised by the late Prof. J. C. Brash, concern nomenclature and illustrations. Many, but not all, of the alterations approved at the International Congress of Anatomy in Paris in 1955 have been accepted in this text. Alternative terms are clearly indicated. Twenty-one drawings have been replaced, and so have many radiographic plates. This familiar manual may be judged lengthy by present-day standards, but it is still, we think, the best available dissection manual. Since so many students today pay little heed to large systematic textbooks, even if they own them, it is all the more desirable that they should use an adequate practical manual. Though the practice of relying wholly or largely upon a dissection handbook is to be deplored, Cunningham's manual is perhaps the best of guide-books to the human body. The new edition is bound in washable material, and preserves its customary handsome appearance.

Cardiovascular Collapse in the Operating Room (London: Pitman Medical Publishing Co. 1958. Pp. 197. 45s.).—Death comes most dramatically in the operating-theatre, partly because of its unexpectedness. It is on this point that the authors of this book, Dr. Herbert Natof and Prof. Max Sadove, of the University of Illinois College of Medicine, have much to say, for the gist of their message is that such deaths are usually assocated with demonstrable disease which should have been detected clinically and suitable precautions taken. Each predisposing cause is carefully considered in a book which will interest surgeons as much as anæsthetists.

Smoking, Lung Cancer and You (London: Lindon Press. 1958. P. 72. 5s.).—This short, easily read book by Dr. Robert N. C. McCurdy presents for the lay reader the main facts concerning the dangers of tobacco-smoking. It is well and interestingly written from a strongly individual viewpoint by a medical officer of health who, after studying the problem of lung cancer both nationally and in his own area, feels that the time has come for Government action. The argument is well documented and doctors as well as laymen should find it helpful in assessing the social and political as well as the statistical aspects of this pressing present-day problem.



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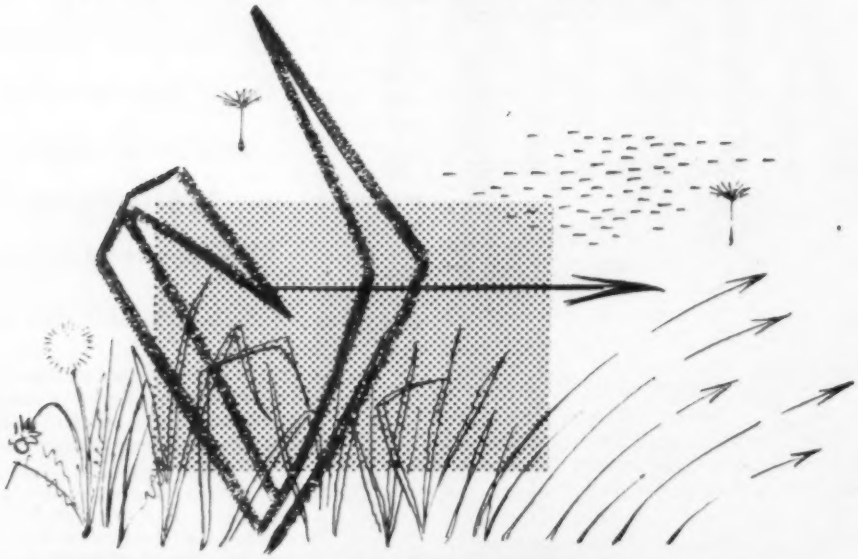

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Heart-lung Machines

SINCE the methods of extracorporeal circulation were first put to clinical use, many rival schools of technique have evolved, each with its ardent supporters. In the early days there was little to choose between them: each had its list of surviving patients, and the causes of mortality were often ill understood; each had its technique to perfect before machines could be accurately compared. There are two fundamental methods of oxygenating blood—by bubbling oxygen through it [1] and by exposing a film of it to oxygen. The film method is subdivided into systems which use rotating discs [2-4] and those incorporating the stationary vertical screen.[5] Though figures have been compiled at each of the big centres using these different methods, a straight comparison between them is difficult for several reasons: the cases may be selected differently, the technical accomplishment of surgeons varies, and their presentation of results is often hard to assess. There is also a hidden factor which bears directly on the success of the operation: the length of time required to close an intracardiac defect must always depend on the dexterity of the surgeon, but the ultimate security of the closure—i.e., freedom from recurrence—may well depend on taking a rather longer time than is commonly required for the intracardiac operation. It has been clearly shown by VARCO et al.[6] that the duration of perfusion at lower rates of flow directly affects the survival-rates of patients. At rates of flow between 56 and 65 ml. per kg. per min. the duration of perfusion was less important, although none of the perfusions lasted longer than an hour. These results with a bubble oxygenator may discourage surgeons from using this type of apparatus, especially in adults. Safety is clearly the first and vital need, but as pressure of work rises other considerations become increasingly important; and ease of cleaning, sterilisation, and maintenance, and manpower demands can all greatly influence the choice of machine.

For these reasons the paper by Dr. GERBODE and his colleagues on p. 284 is of much interest. It is an account of the clinical use by one surgeon of two filming machines using different principles: one a fixed vertical screen, a variant of the Gibbon, developed by OSBORN [7] in San Francisco; the other the rotating-disc oxygenator devised by MELROSE [2] at the Postgraduate Medical School and introduced into the operating-theatre at Hammersmith Hospital five years ago. Dr. GERBODE had previously decided that the film oxygenator was preferable to the bubble type. Now, since "no substantial difference in mortality or morbidity or any other measurable variable could be detected", considerations of convenience, cost, and administration have made Dr. GERBODE decide on the use of the Melrose machine only in future at Stanford University Hospital. In the cases recorded the original Melrose 'Perspex' oxygenator [2] was used. The material of the oxygenator and of the discs is now to be changed to permit autoclaving and the disposal of the discs: "these requirements are judged essential for the proper maintenance and safety of an apparatus used more than five times a week". This sentence may give a clue to one of the essentials for excellence in this work: for their successful performance these complex procedures require a frequently repeated, routine, standardised technique.

The paper from Stanford University, with its account not only of the advantages of the British machine but also of the routine safe use of elective cardiac arrest—another British advance—shows that British surgery has contributed generously to the common fund of knowledge in intracardiac surgery. It illustrates too how the provision of an efficient machine does not by itself ensure successful open-heart surgery. More important now is a highly trained medical and surgical team working with unremitting diligence, and having at its disposal ample means for preoperative investigation, first-class operating-theatre equipment and accommodation, and adequate provision for the immediate postoperative recovery period and later convalescence. Dr. GERBODE and his colleagues are to be congratulated on the figures they present. The series is not long by American standards but it is long enough to be entirely convincing. It is notable that he has lost only 3 out of 14 patients treated by an intracardiac operation for the tetralogy of Fallot, and some of the other complicated defects have been very successfully dealt with. We are glad to publish a record of this project which has been brought to so satisfying a conclusion by a joint team of American and British workers.

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Hæmolytic Disease of the Newborn

IN the past ten years the infant mortality in England and Wales has fallen by half, largely owing to the improved treatment of infective illness. Today 80% of neonatal deaths are due to causes, such as immaturity and congenital deformity, which cannot yet be prevented. Consequently the 350 deaths due to hæmolytic disease assume considerable importance. It can be calculated that this disease also accounts for 500 of the 16,000 stillbirths each year.

Since the discovery of the rhesus factor by LANDSTEINER and WIENER [1] in 1940, great strides have been made in the understanding and management of this disease; and it is claimed that, with early diagnosis and exchange transfusion in selected cases, over 95% of affected infants that are born alive should survive.[2 3]

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Yet there has been no substantial fall in mortality. Indeed it is estimated that some 200 infants die needlessly each year, and this was confirmed by WALKER and MOLLISON [4] in a study of deaths attributed to hæmolytic disease in England and Wales in the years 1953 and 1955. No new knowledge is required to prevent this loss of life—only the application of existing knowledge, which is set out in a memorandum of the Central Health Services Council which is being sent to all family doctors.[5] But hæmolytic disease not only contributes to the total of fœtal and neonatal deaths: it carries important, often poignant, implications for the families concerned. Therefore, though the risks of immunisation are small, even the first pregnancy in an Rh-negative woman calls for special obstetric care.

The importance of early diagnosis is now recognised, and the memorandum outlines a policy of blood-grouping tests designed to ensure antenatal prediction. But, since this will not always be achieved, it draws attention to the early symptoms which point to the diagnosis.

The measures recommended include the Rh grouping of all pregnant women and antibody tests at 32–36 weeks of pregnancy in all found to be Rh-negative. The collection of clotted cord blood from the infants of all Rh-negative women is also recommended, since a positive Coombs test will establish a diagnosis of hæmolytic disease. (On the other hand a negative result does not exclude all forms of this disease.) An alternative plan for antenatal prediction consists in the testing of all mothers for antibodies between 32 and 36 weeks of every pregnancy. It is claimed that by this plan, as one specimen is required from every mother in every pregnancy, testing is less likely to be overlooked, while a few cases of immunisation to rare antigens are detected antenatally. Which policy is followed will depend largely on local arrangements.

The memorandum rightly points out that jaundice in the first twenty-four hours of life is to be ascribed to hæmolytic disease until proved otherwise, and demands immediate admission to hospital. This applies even if the infant is firstborn, and even when the known blood-group background appears to exclude the diagnosis. If in addition there are pallor, bruising, enlargement of the liver, or other signs, admission is urgent. Jaundice appearing after the first day of life can sometimes become so intense as to cause brain damage; therefore deep jaundice in the first week of life requires expert opinion. Hæmolytic disease due to ABO incompatibility has been recognised with increasing frequency in recent years,[6 7] but no single test establishes the diagnosis—the Coombs test is often negative. Antenatal prediction cannot be achieved with certainty, and consequently diagnosis is usually based on the results of many tests that are not easily interpreted. The true incidence is not known. VALENTINE [8] has studied a series of infants showing jaundice in the first day of life. In all cases there was an underlying hæmolytic anæmia; in a third this was Rh hæmolytic disease of the newborn, and in the remainder hæmolytic disease due to incompatibility within the ABO groups. Some workers claim that ABO hæmolytic disease is commoner than that due to rhesus factor, but, being milder,[9] presents a less important practical problem.

As the memorandum says, results are best in units with special experience, and if a unit is to provide really effective service it must carry out the necessary tests at any hour and be able to undertake transfusion within half an hour of birth. (We hope the statement that the "interval between birth and exchange transfusion should be as brief as possible" is not misinterpreted; for such urgent treatment is required only in very severely affected infants, and in most it is better to apply this treatment between four and eight hours after birth.) A calculation based on the fatal cases in 1953 and 1955 [4] showed that each hospital concerned dealt, on average, with only twelve cases a year, whereas the memorandum suggests that to maintain the required standard each unit should deal with at least fifty cases a year.

A national trial reported in 1952 [10 11] suggested that spontaneous delivery resulted in less loss of life, fœtal and neonatal, than did routine premature induction. But experience has justified premature induction in families where a preceding infant has been very severely affected or stillborn. Some workers go further and recommend induction for all cases of Rh isoimmunisation,[12–14] but such a policy should not be adopted hastily. It could prevent at most sixteen stillbirths in a hundred cases treated in this way, against which must be set the risks of induction to both mothers and infants. In fact probably only eight stillbirths would be prevented; for almost half occur before 35 weeks gestation, the time most commonly recommended for induction. If on the other hand stillbirth could be forecast with relative certainty, induction would be justified, for there is no convincing evidence that cortisone or any other drug is of value in this condition.

There is a correlation between maternal antibody titre and severity,[15] but it is doubtful whether this is so precise as to help in the management of individual cases. WALKER [16] claims that tests on liquor amnii enable severity to be forecast. This work requires confirmation and elaboration; but, alone or together with antibody titre, such tests may prove of real practical value.

Many problems may remain; but if the recommendations of the memorandum are applied the coming years may see as big a change in the mortality of hæmolytic disease of the newborn as antibiotics have brought about in some other diseases.

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The Development of Respirators

IN 1947 Britain had her first big epidemic of poliomyelitis. There were about 600 Both-type tank respirators in the country at that time, presented by Lord NUFFIELD in 1938–39, and they were invaluable for patients with respiratory weakness; but the epidemic revealed how inadequate were the country's resources for dealing with poliomyelitis. Apart from a dearth of doctors and nurses with the necessary experience, the design of respirators had failed to advance with the times, and, what was worse, many respirators had become useless from lack of maintenance. Consequently, in 1948, the design of respirators attracted much interest, and the progress of the past ten years is now reviewed in the Medical Research Council's report.[1]

Tank respirators have not changed in principle, but improvements in detail have been of great practical importance. A choice of respiratory-rates was provided, more ports were placed in the side of the tank, and an inflator was included so that artificial respiration could be continued when the patient was withdrawn from the tank for nursing care. When a patient was being put into an old respirator his head had to be delivered through a small opening in the front of the tank, a very cumbersome business, which was avoided by splitting the front into an upper half which could be raised and lowered, and a lower half which was fixed. This great practical advance was introduced as one of a number of modifications to the Both respirators, which were thereby given a new lease of life. The principle of splitting the front of the tank was carried to its logical conclusion by the development of an "alligator" respirator, first designed in Australia by BOTH and now made by at least two manufacturers in the United Kingdom. In this the whole respirator is split horizontally and hinged at the foot, so that access to the patient is easy and the respirator can be brought into action again merely by closing the lid.

Cuirass respirators which fit over the abdomen and chest have also been designed, and, though as respirators they leave much to be desired, their convenience makes them useful for the patient who needs respiratory assistance for part of the day or while asleep. The Tunnicliffe breathing jacket [2] is a similar device that provides more efficient artificial respiration at some cost in convenience. A rocking bed is also in production and is specially suitable for weaning from artificial respiration those patients whose diaphragms have not recovered.

The fundamental novelty of this period has been the introduction of intermittent positive-pressure respiration (I.P.P.R.) in Denmark in 1952. A rubber or sometimes metal tube is inserted through a tracheotomy, and an inflatable cuff around the tube ensures a good fit in the trachea, so that foreign material in the pharynx cannot get into the lungs, and air blown into the lungs cannot escape through the nose and mouth. A tracheotomy is now considered essential in any patient with paralysis of swallowing as well as of respiration, and those with experience of acute paralysis increasingly favour a tracheotomy when in doubt. In the presence of a tracheotomy I.P.P.R. is, in Europe at least, the usual means of artificial respiration. Many positive-pressure respirators have now been designed with many different characteristics, and the most prominent of their merits should be robustness and reliability. In I.P.P.R. each respiration resembles a miniature Valsalva manœuvre in which the intrathoracic pressure is temporarily raised. There is good evidence that in very sick animals this can reduce the venous return to the heart, and that this effect can be reversed by applying negative pressure between inspirations. Some of the more recent I.P.P. respirators provide a negative-pressure phase, and clinical evidence should soon be forthcoming about their efficacy.

It seems likely that the stage of intensive development of breathing machines is coming to an end, and that future research will deal with the physiological state of the patient receiving artificial respiration. A wide subject for inquiry is open here, dealing not only with the exchange of oxygen and carbon dioxide in the lungs but also with the mechanics of the lungs and chest wall, with particular reference to the effects of pressure changes on the circulation.

1. Report of the Medical Research Council for the year 1956–57. H.M. Stationery Office. Cmd. 453. 13s.
2. Spalding, J. M. K., Opie, L. *Lancet*, 1958, i, 613.

Annotations

CANCER OF THE TONGUE

ONE of the problems that is likely to beset any surgeon interested in the operative treatment of cancer of the tongue is the small number of cases that come his way.[1] This is, happily, one of the sites where the incidence of cancer seems, certainly in civilised societies, to be declining steeply—a fact difficult to reconcile with the view that cancer of the mouth and of the bronchus share tobacco as a common ætiological factor. Added to this, there is an increasing tendency for all patients with mouth cancer to be channelled to the radiotherapist for their primary treatment. Accordingly it is surprising to read in the opening sentence of an appraisal of progress in surgical therapy by Danely P. Slaughter and his colleagues [2] in the University of Illinois: "Somewhat over a decade has now elapsed since the surgical treatment of cancer of the tongue assumed a pre-eminent position in the over-all management of this disease." Later they admit that there is still little published evidence to sustain the claims of the surgeon in this field; but they cite unpublished data claiming a 36% five-year-cure rate in a small group of patients with regional lymph-node metastases.

In the management of the tumour at the primary site the place of surgery is very much a matter of opinion; but to the view that, in general, neck metastases are best dealt with by block dissection radiotherapists usually subscribe. Rather less than half the patients will be found at the outset to have no enlargement of the neck nodes; and in this type of case the expectant policy seems, in the main, to prevail; but Tailhefer,[3] from his very wide experience at the Fondation Curie, stated a strong case for prophylactic operation, claiming that his results were improved by this more energetic attack. It has now been

1. Shedd, D. P., Schmidt, N. L., Chang, C. H. *Surg. Gynec. Obstet.* 1958, **106**, 15.
2. Southwick, H. W., Otten, J. W., Slaughter, D. P. *Surgery*, 1958, **43**, 313.
3. Tailhefer, A. *Proc. R. Soc. Med.* 1952, **45**, 757.

shown that, even where no enlarged nodes can be felt in the neck, in 40–60% of cases the nodes will be found at operation to contain microscopic metastases.[3–5]

Surgical enthusiasts such as Hayes Martin[6] are now inclined to pin their faith in the cure of lingual cancer to a combined en-bloc resection of the primary tumour and the regional lymph-nodes, whether these are clinically involved or not; but he and his colleagues have displayed a not unnatural reluctance to practise prophylactic block dissection, believing that the risk of ultimate contralateral spread is 11%. Slaughter[7] may be presumed to favour a more vigorous approach, since he believes the risk of such a happening to be less than 1%.

Surgeons admit that this, or indeed any other, type of operation can have no place in the treatment of cancer of the posterior third of the tongue. Moreover, even when surgery is undertaken under the most favourable circumstances, the chances of disappointment are considerable. An apparently happy result is all too often marred by the appearance of a new primary (perhaps in 1 in 10 or more [7 8]), or a carefully conducted dissection is followed by the early appearance of seedling "recurrence" in the operation field. In the prevention of this, there is perhaps relevance in the work of Southwick and Cole,[9] who in a careful study of the risk of local implantation following colon resection for cancer, showed very clearly the merit of scrupulous care in avoiding spillage of cancer cells.

Consideration of the contending claims of surgery and of radiotherapy in the control of cancer of the tongue (or, for that matter, at any site in the mouth) is hampered by the lack of any good evidence on the usefulness of the two methods in comparable cases. It is high time that exponents of the two approaches provided a firm answer based on shared experience.

FAILURE OF DETERGENTS TO DISINFECT

IN 1935—the year in which he discovered that 'Prontosil' could cure experimental infections—Domagk described the first of a new class of surface-active chemicals with detergent and bactericidal properties. The cationic members of this class are now widely used as disinfectants, and the most useful of them are the quaternary ammonium compounds. It was very soon apparent that some organisms are sensitive to the sulphonamides and others resistant, but even now it is not always realised that there are similar differences in sensitivity of different bacteria to the action of the quaternary ammonium disinfectants. Gram-positive cocci are much more sensitive to these agents than are gram-negative bacilli; *Pseudomonas pyocyanea* is relatively resistant. In practice these disinfectants are used at concentrations which should suffice to kill even less sensitive bacteria, but under working conditions the effective concentration or the time of exposure may be so reduced that *Ps. pyocyanea* will not be destroyed. Plotkin and Austrian[10] have described the consequences of such a failure in disinfection.

Fifteen patients in a New York hospital developed septicæmia after receiving intravenous transfusions. Blood-cultures from every patient yielded the same organism—an unusual bacillus closely related to *Ps. pyocyanea*. This finding prompted a full investigation of all materials used in intravenous transfusions, and it was found that swabs for disinfecting the skin before injection, which were stored in disinfectant, were contaminated with the same organism. The disinfectant was a 0·1% solution of 'Zephiran', a quaternary ammonium compound widely used in North America. Before each intravenous injection the skin had been smeared with what was in effect a culture of live bacteria. It is known that cationic detergents are adsorbed readily to cotton fibres,[11] and this appears to have been the way in which the concentration of zephiran was reduced below that necessary to kill *Ps. pyocyanea* and related bacteria. Last year Keown et al.[12] reported five deaths from *Ps. pyocyanea* septicæmia after cardiac operations, the source of the infection being a heart-lung machine supposedly sterilised with 0·1% zephiran.[12] Lowbury cultured *Ps. pyocyanea* from bottles of 1% cetrimide in use in a British hospital.[13] The organisms survived in the corks, and substitution of screw-caps for corks in disinfectant bottles greatly reduced the number of *Ps. pyocyanea* infections in this particular hospital. Anderson and Keynes[14] have shown that extraction of the cork releases a shower of infected cork dust into the bottle. Organisms from this dust may cause wound infection if the disinfectant is used immediately after being poured out—before the organism has been exposed to disinfectant long enough to be killed.

Practical lessons may be learnt from these mishaps. Disinfectants should not be dispensed in bottles with corks. Gauze and cotton-wool swabs should not be sterilised and stored in disinfectant but should be sterilised in a pressure-steam steriliser. Complex apparatus which cannot be heated is probably best sterilised with ethylene-oxide gas.[15] Quaternary ammonium compounds are not very satisfactory skin disinfectants. As we pointed out some years ago, the most effective disinfectant for this purpose is still 2% iodine in 70% spirit.[16]

In short, quaternary ammonium disinfectants should be used with some discretion, in the knowledge that in their action on bacteria they resemble the sulphonamides more than the autoclave.

HOMOTRANSPLANTATION OF THYROID IN UNIOVULAR TWINS

WHEN it became evident that myxœdema and cretinism were due to thyroid deficiency the first proposal for treatment was that a healthy thyroid should be transplanted into the affected person. Horsley[17] in 1890 suggested that the thyroid of a sheep might be used for this purpose, and this suggestion was carried out by Bettencourt and Serrano[18] in the same year. Horsley[19] recorded that even earlier both Bircher and Kocher had treated cachexia strumipriva by implanting fragments of goitre from another person into the patient's abdominal cavity. We now know that attempts to graft tissue from another species, or even from another human being, are immunologically futile.

As would be predicted, these early transplantation experiments were followed by only temporary clinical improvement, and their only importance is that they led directly to Murray's demonstration of the effectiveness of thyroid extract in the treatment of myxœdema. When tablets of dried thyroid extract came into common use, interest in the possibilities of transplantation lapsed. It seemed difficult to imagine any treatment simpler and

4. Lyall, D., Schetlin, C. F. *Ann. Surg.* 1952, **135**, 489.
5. Roux-Berger, J. L., Baud, M., Courtial, J. *Mém. Acad. Chir.* **75**, 120.
6. Martin, H. Surgery of Head and Neck Tumours. London, 1958.
7. Wood, C. A. P., Boag, J. W. Researches on the Radiotherapy of Oral Cancer. *Spec. Rep. Ser. med. Res. Coun. Lond.* 1950, no. 267.
8. Slaughter, D. P., Southwick, H. W., Smejkal, W. F. *Cancer*, 1953, **6**, 963.
9. Southwick, H. W., Cole, W. H. *Surg. Clin. N. Amer.* 1955, **35**, 1363. See *Lancet*, 1956, i, 944.
10. Plotkin, S. A., Austrian, R. *Amer. J. med. Sci.* 1958, **235**, 621.
11. Glassman, H. N. *Bact. Rev.* 1948, **12**, 105.
12. Keown, K. K., Gilman, R. A., Bailey, C. P. *J. Amer. med. Ass.* 1957, **165**, 781.
13. Lowbury, E. J. L. *Brit. J. industr. Med.* 1951, **8**, 22.
14. Anderson, K., Keynes, R. *Brit. med. J.* 1958, ii, 274.
15. Skeehan, R. A., King, J. H., Kaye, S. *Amer. J. Ophthal.* 1956, **42**, 424.
16. *Lancet*, 1952, i, 250.
17. Horsley, V. *Brit. med. J.* 1890, i, 287.
18. *Sem. Med.* 1890, **10**, 294.
19. Horsley, V. *Brit. med. J.* 1890, ii, 201.

more completely effective than oral replacement therapy. Yet fatal cases of myxœdema still occur [20]; the usual sequence of events seems to be that patients correctly diagnosed and treated in the first instance become careless in time about taking their tablets and eventually pass into a state of severe myxœdema which is therapeutically irreversible. For the most part such cases have occurred in people living alone with no-one at hand to remind them of the need for taking tablets. It is evident that a successful thyroid graft would be a complete protection against this unhappy sequence of events, and it therefore seems worth reviewing again the possibilities of transplantation.

The work of P. B. Medawar and his school on immunological tolerance has shown that homotransplants have no hope of survival unless the recipient has been prepared by the injection of the relevant antigens during fœtal or very early postnatal life. How early this would have to be in man is uncertain, but a homotransplant might possibly survive if implanted in the first few weeks of life. It is unfortunately difficult to diagnose cretinism at any age less than about 3 months, but the combination of astute clinical observation and modern tests of thyroid function might establish the diagnosis in a few isolated cases. If this could be done before the patient reached the age of 1 month, transplantation of a piece of thyroid from another person might be worth attempting.

At any later age homotransplants will certainly fail to take, with the single exception of one taken from an identical twin. Fortunately when one uniovular twin is cretinous the other is usually normal; and this was so in the case described by Harnack et al.[21] The healthy twin, Marina, had a normal uptake of radio-iodine; but her cretinous sister, Christiane, had only a trivial uptake in a minute fragment of thyroid tissue at the base of the tongue. When the twins were $7^1/_2$ years old the greater part of one lobe of Marina's thyroid was removed at operation and inserted in two pieces in Christiane's neck, one on each side, deep to the sternomastoids. The early clinical effects were not striking, and three months after the operation Christiane again required oral thyroid treatment. But a year later, thyroid was stopped without an immediate decline into hypothyroidism. Radio-iodine tests after administration of thyroid-stimulating hormone showed that the child now had useful, though still greatly subnormal, thyroid function. It seems likely that the bulk of the implanted thyroid must have died shortly after the operation, but that enough remained for regeneration to occur. Further observation will be required before we know whether the fragments will supply all the child's requirements of hormone.

ENTEROPATHOGENIC ORPHANS?

IN 1956 a conference was held in New York on Viruses in Search of Disease [22]—an unusual topic. It is, in fact, an important one, because so many viruses are now being isolated from the intestines of healthy people. 47 of these "enteroviruses" [23] are known—3 types of poliovirus, 19 of Coxsackie A, 5 of Coxsackie B, and 20 of the enteric cytopathogenic human orphan (ECHO) group—and there is no reason to think that the list will end here. Some are already firmly associated with disease: poliovirus, Coxsackie virus, and some types of ECHO virus which cause aseptic meningitis. Ramos-Alvarez and Sabin [24] have studied their association with summer diarrhœa of infants and very young children.

They describe an epidemiological study in which a comparison was made between the viruses and bacteria isolated from the fæces of 153 children with diarrhœa and of 100 healthy children of the same age, district, and socio-economic background. Material from rectal swabs was used to inoculate monkey-kidney tissue cultures and newborn mice. Cultures were also made for pathogenic bacteria, and paired sera were tested from 24 of the patients who had positive stools. While enteroviruses were isolated from 20% of the healthy children, they were present in about 50% of those with diarrhœa. This difference lay largely with the ECHO viruses, which were six times commoner in the test group than in the controls. The prevalence of poliovirus and Coxsackie virus (about 3%) was the same in both groups. 7% of the patients carried salmonella or shigella, which were not isolated from the healthy children; but there was no significant difference in the rates for pathogenic strains of *Escherichia coli*. In all the cases where the serum was examined there was a rise in titre to the virus which was isolated from the rectal swab. This proves that the virus in the fæces was causing an active infection when the child was ill, but does not prove that this infection was the cause of the symptoms.

The evidence in this paper certainly suggests that the ECHO viruses may be a cause of summer diarrhœa. But great care has to be taken before claiming that an enterovirus is a cause of disease. These agents are isolated so often from healthy children that it would be surprising if they were not found also in the fæces of those with diarrhœa from other causes. Mixed infections may occur, or infection with agents which we cannot detect by existing techniques. It is difficult to exclude completely the possibility that viruses may arise from the cells or serum used in the tissue culture. Yet another difficulty lies in the nature of the disease. As Ramos-Alvarez and Sabin remark, "Summer diarrhœa of very young children is not a clinical entity but rather a consequence of transitory infection with a large variety of bacterial and viral pathogens." Even in the ECHO group no particular type seems to be associated with the disease. In this study the viruses isolated were distributed among thirteen different serological types. But Ramos-Alvarez and Sabin cite an outbreak of diarrhœa among infants in hospital described by Eichenwald et al.[25] which was apparently caused solely by ECHO virus type 18. Possibly when we know more about the group some epidemiological pattern may emerge, as it has with the staphylococci and pathogenic *Esch. coli*.

The first report of the committee on the ECHO viruses in 1955 [26] stated that, as soon as one of these viruses was established as the cause of a clinically distinct disease, it should be removed from the group—which is probably a heterogeneous one anyway. Although associations are being demonstrated between ECHO viruses and disease, they do not appear to be clear-cut enough to justify the removal of these agents from the "orphanage". The name ECHO has been acquiring a meaning in its own right as the meaning of the initials is forgotten [27]; it seems likely that the name "orphan viruses", applied by Duran-Reynals "at a moment of conviviality",[26] will persist.

20. *Lancet*, 1956, ii, 768.
21. Harnack, G. A., Horst, W., Lenz, W., Zukschwerdt, L. *German med. Monthly*, 1958, **3**, 172.
22. *Ann. N.Y. Acad. Sci.* 1957, **67**, 209.
23. Committee on Enteroviruses of the National Foundation for Infantile Paralysis. *Amer. J. publ. Hlth*, 1957, **47**, 1556.
24. Ramos-Alvarez, M., Sabin, A. B. *J. Amer. med. Ass.* 1958, **167**, 147.
25. Eichenwald, H. F., Ababio, A., Arky, A. M., Hartman, A. P. *ibid.* 1958, **166**, 1563.
26. Committee on ECHO viruses of the National Foundation for Infantile Paralysis. *Science*, 1955, **122**, 1187.
27. Andrewes, C. H., Sneath, P. H. A. *Nature, Lond.* 1958, **182**, 12.

Occasional Survey

BIOCHEMICAL CONCEPTS OF SCHIZOPHRENIA *

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THE demonstration of the organic basis of general paralysis led, about fifty years ago, to the hope that schizophrenia might also prove to be caused by some easily distinguishable organic agent or condition. The discovery that psychoses or mental deficiency could be caused by avitaminosis, hormonal imbalance, and specific disorders of metabolism, such as phenylketonuria, lent weight to the belief that schizophrenia might also be due to some metabolic or endocrine disorder; but the persistent failure to demonstrate any such organic basis led to a slackening of the momentum behind this approach and to the gradual dominance of the belief, among psychiatrists in North America at any rate, that the ætiology of schizophrenia was essentially psychological.

A physiological interpretation of this psychological hypothesis may be put as follows: everyone would agree that severe emotional trauma can lead to behavioural disturbances. The psychological theories hold that schizophrenia may be explained by a logical extension of this, coloured by the discovery that emotional and other allied psychological factors can continue to interact and to act as causal agents when they are no longer present in consciousness, for this is what the Freudian theory of the unconscious amounts to. Psychoanalysis holds that the causes of the illness lie in faulty early training and interpersonal relationship. Its physiological basis is supposed merely to consist of those mechanisms whereby *any* past experience affects present emotional experience, motivation, and behaviour, reacting in this case to an involved and scarifying series of noxious experiences. The warping of the child's psychological development is held to be a sufficient explanation of the adult schizophrenic. The schizophrenic is withdrawn *because* the early environment forced the child to withdraw, and no specific metabolic fault is held to be involved.

However, we now have a considerable body of evidence against this hypothesis, for organic changes have been discovered in schizophrenia that are certainly relevant to its ætiology, and progress has been made in constructing plausible hypotheses to explain these biochemical and pathological findings; but this does not lead us to reject the importance of psychological factors, as we shall see.

The evidence for a genetic cause of schizophrenia is now generally agreed to be overwhelming, although the exact details may not yet be known. Kallmann (1953) has accumulated a large body of evidence favouring the hypothesis that single-factor inheritance of the recessive type is the genetic cause of schizophrenia. There are also more specific physiological findings. The metabolic theories of schizophrenia have been focused on the idea of some cerebral toxin produced by faulty metabolism. Equally possible are the lack of a necessary factor and the imbalance between two complementary mechanisms.

* Based on seminars held at the University of Iowa, March 1, 1958, and at Emory University, April 29, 1958.

An early proponent of such a view was Jung (cited by Osmond 1957) with his " toxin X ".

Mann and Quastel (1940) proposed that a toxic amine might be responsible, and a popular idea of that time was that toxic amines from the gut might be involved—an idea that did not prove fruitful in this field but has found application in another following the work of Sherlock et al. (1954), who showed that venous blood derived from the gut and bypassing the liver can produce psychotic effects.

Buscaino (1952) introduced the concept of a toxic indole as causing schizophrenia, which idea is again fashionable.

Broad Biochemical Investigations

In the absence of any specific directing hypothesis a large number of biochemical investigations were made on a wide front in the hope of turning up some clue that might suggest the cause. Many of these reports were negative or contradictory, and the validity of others was doubtful either because the tests used were unreliable or because the findings might well be explained by the poor diet, concomitant medication, lack of motility, &c., of schizophrenics.

Out of all this work the only findings that seem reliable are as follows:

(1) *Liver function.*—Richter (1957) states that there appears to be some impairment of liver function in schizophrenics as a whole, but there is no evidence that it is an invariable or obligatory concomitant. However, Richter emphasises the possibility that different enzyme systems in the liver may be affected to different degrees, and concludes that we cannot yet exclude the possibility that in schizophrenics some of the functions of the liver may be seriously impaired.

(2) *Toxicity of body fluids.*—The blood of schizophrenics has been reported to be toxic to tadpoles (Fischer 1953) and to fibroblasts grown in tissue culture (Fedoroff and Hoffer 1956), but the latter workers find a similar degree of toxicity in patients undergoing surgery, suggesting that a non-specific response to stress of the kind described below may be involved. Reider (1957), using Witt's elegant spider-web technique, has shown that extracts from schizophrenic urine produce significant abnormalities in the web-spinning behaviour of spiders similar to those produced by hallucinogens.

(3) *Reaction to stress.*—Various measurements have been made of the response (pulse-rate, blood-pressure, skin circulation, and response to adrenaline) to stress (Finkelman and Stephens 1936, Pfister 1938). These show that chronic schizophrenics are less reactive than healthy people. Increased excretion of 17-ketosteroids has been found only in paranoid schizophrenia (Sands 1957).

(4) *Circulatory system.*—Careful observations have shown that schizophrenics exhibit a mild but consistent degree of hypotension and a constriction of the small arterioles of the skin, leading to cyanosis (Shattock 1950). This is also evidence of a disorder of capillary structure (Lovett Doust 1955).

(5) *Metabolism of nitrogen.*—Nitrogen is retained in recurrent catatonia, but this condition is rare and may not be related ætiologically to the bulk of cases of schizophrenia.

(6) *Metabolism of phosphorus.*—Örström and Skaug (1950) found a diminished turnover of adenosine triphosphate in schizophrenics, and Örström (1951) reported a higher content of phosphoglycollic acid in their red blood-cells.

(7) *Abnormalities in brain.*—This work is still in its early stages, but Ashby (1950) has reported that the activity of carbonic anhydrase is abnormal in schizophrenia. Normally the activity of this enzyme is greatest in the occipital cortex and least in the temporal region, but in schizophrenia the normal topographical pattern was obliterated, except in some early cases, where there was a reduction in the frontal region. Birkhauser (1941) reported a lower activity of monoamine oxidase than normal in the pallidum of schizophrenic subjects.

(8) *Homœostasis.*—If a large series of measurements is made of basal metabolic rate, circulation-rate, body temperature,

excretion of 17-ketosteroids, thyroid activity, and water metabolism in schizophrenics and in healthy people, it will be found that the variance of these readings will be greater in the schizophrenics. This suggests that a concomitant of schizophrenia is some disorder of homœostasis.

(9) *Other disorders* have been reported, such as disordered excretion of various substances in the urine—e.g., sulphur compounds (Koch and Mann 1909), phenolic derivatives (Richter 1957), indoles (Riegelhaupt 1956), imidazoles (Stewart 1930), and aromatic substances (McGeer et al. 1956)—but this very variety suggests that these compounds arise from increased bacterial action in the gut from some local cause such as stasis rather than a specific metabolism of schizophrenia.

In summary, therefore, those investigations not directed by a specific hypothesis lead only to the certain deductions of a disordered response to stress, a disordered homœostasis, a probably non-specific toxicity of body fluids, a disorder of nitrogen metabolism in a certain rare kind of schizophrenia, and specific disorders of phosphorus metabolism and of cerebral carbonic-anhydrase and amine oxidase function. These empirical findings do not suggest any specific theory but only that the biochemical mechanisms of the response to stress and of homœostasis are involved.

First Specific Biochemical Theory

The first specific [1] biochemical theory of schizophrenia was put forward by Osmond and Smythies (1952) and was stated in a more specific form by Hoffer et al. (1954).

Search for Toxic Metabolite

These workers applied a form of Koch's postulates adapted to a metabolic illness. These postulates require us to isolate from schizophrenics a metabolite which, injected into healthy people, would reproduce the symptoms of schizophrenia. This metabolite should either be found de novo in schizophrenics, or at least in significantly larger amounts in schizophrenics than in healthy people, or possibly the schizophrenic may be abnormally sensitive to the metabolite. Contributory evidence should be obtained by showing other toxic properties of the metabolite or by testing for its presence in a deductive manner.

But what metabolic fault should one look for in schizophrenia? There are millions of possible faults—which one should we choose? We approached this problem by asking a series of questions. The first was: What known chemicals are there that produce in healthy people effects closest to the symptoms of schizophrenia? We delineated a class of chemicals, including mescaline and lysergic acid diethylamide (L.S.D.), that had this property and we called them "hallucinogens". We did not claim that these compounds produce exactly the signs and symptoms of schizophrenia. The differences in temporal and situational factors will always preclude the exact matching of an experimental and a natural psychosis. However, for our purpose what was required was the closest known analogy.

We next asked which of these substances or any substance nearly related thereto could conceivably be formed in bodily metabolism, and we pointed to the close chemical relationship between mescaline and adrenaline, which suggested that derivatives of adrenaline might be strong candidates for the role of "M substance"—the mescaline-like toxin of schizophrenia. Our hypothesis does not necessarily involve indoles except in so far that certain metabolites of adrenaline are indoles; our hypothesis is specifically directed towards metabolites of adrenaline and allied compounds.

Harley-Mason (cited by Osmond and Smythies 1952) suggested one specific mechanism whereby a closer mescaline analogue than adrenaline could be produced in the body—i.e., methylation of the phenolic groups of adrenaline—a reaction that Axelrod (1957) has found taking place in the body. The finding by Resnick et al. (1958) that adrenaline is *predominantly* detoxified by *o*-methylation in humans brings Harley-Mason's hypothesis of an excessive methylation back into prominence. A possible fault might be the production in schizophrenia of the possibly psychotomimetic dimethoxy derivative of adrenaline. The comparative amount of *o*-methylation in schizophrenics and normals should be measured: a lesser degree in schizophrenics might suggest that some of the adrenaline was being metabolised by the adrenochrome pathway. This hypothesis could easily be tested.

Adrenochrome

Dr. Eric Asquith, an anæsthetist at Regina General Hospital, told us that he had obtained psychotic reactions by giving patients injections of "pink adrenaline," which is a red mixture of oxidised products of adrenaline. Since then Hoffer and Osmond (1958) have made an extensive study of a psychosis lasting a month and produced by the self-administration of "pink adrenaline" (to which adrenaline turns slowly on mere exposure to the air) for this length of time by an asthmatic; and H. E. Himwich (personal communication) has told us that he has observed an injection of adrenaline 1 mg. to produce severe temporary personality changes of a paranoid type in a healthy person. So we suggested that M substance might be adrenochrome, adrenolutine, or some other close relation among the many closely allied immediate oxidation products of adrenaline. This hypothesis led to a number of experiments and observations.

Some solutions of oxidation products of adrenaline have been reported to produce psychological disturbances in healthy volunteers, whereas others did not. The difficulty here is that adrenochrome is very unstable and extremely reactive. Thus in most cases it is probable that a mixture of substance has been injected and that adrenochrome is quickly changed into other substances once it gets into the body.

Hoffer (1957a) has published observations on the more stable adrenolutine (trihydroxy N-methyl indole, an isomer of adrenochrome). By a double-blind technique he tried to determine which persons had had the adrenolutine and which had had the placebo.

This he was unable to do at first as the P value of his result was only 0·1. In a later experiment (Hoffer 1957b) he succeeded in doing this with a P value of 0·02. However, in a third experiment (Hoffer 1957b) done in the three months following the last experiment, he again failed to make a significant prediction. This probably means that the adrenolutine had deteriorated by this time; but of course, strictly speaking, chi-square should always be calculated for the whole of such a series to avoid the charge of selection of data. Chi-square for the whole series did not reach significant values ($P=0{\cdot}2$), but the majority of successful predictions came during the first month, thus suggesting a deterioration of the adrenolutine. Hoffer is repeating these experiments, using a pure sample of adrenolutine.

Another difficulty is one common to all tests that may be made of any drug to see whether it produces symptoms resembling psychosis, and that is the design of the experiment.

1. Where a single compound, or a *small* group of compounds, or a specific biochemical mechanism is specifically implicated in the causation of schizophrenia.

Pilot experiments will be needed to test the range of the apparently effective dose, to look for the type of response to expect, and to spot any undesirable complications. The actual evaluation of psychotomimetic properties of a drug then depends on a properly designed double-blind experiment in view of what we now know of the extraordinary range of placebo reactions that can occur (Trouton 1958). Now that the pure forms of these compounds are, through the efforts of Heacock et al. (1958), at last available, we can proceed to properly designed evaluation of stable compounds in the adrenaline oxidation series.

Gastaldi et al. (1957) were unable to produce such symptoms with pure adrenochrome, but they did not appear to use the careful psychological testing methods of Hoffer (1957 and b).

We found no change in behaviour in mice, even after such a large intraperitoneal dose as 40 mg. per kg. of body-weight, and S. Martens (personal communication) has found none in monkeys.

Species differences are important in this field, however, particularly in the case of those higher social, intellectual, and emotional functions that are affected in schizophrenia and hardly play any prominent part in the lives of mice or even monkeys. Possibly the enzyme systems that control these higher functions may hardly be developed in the lower mammals. Thus evidence from non-human sources about substances producing symptoms resembling psychosis needs to be assessed with caution. However, it is quite possible that adrenochrome is not such a substance but that one of its precursors or derivatives may be.

The work of Professor P. Holtz and Dr. G. Taubmann (personal communication) has thrown some light on this. They have found that freshly prepared adrenochrome does not produce symptoms resembling psychosis; but, if it is first oxidised by shaking with normal human serum in air, the resultant liquid (deproteinised) will produce symptoms of psychosis if given sublingually. Furthermore, pure adrenochrome does not inhibit glutamic-acid decarboxylase whereas the oxidised form is a potent inhibitor of this important enzyme which produces the aminoacid G.A.B.A. (γ-aminobutyric acid) thought to be concerned with synaptic inhibition in the brain. This is the first confirmation to date of the work of the Saskatchewan group on humans.

Schwarz et al. (1956) report that intraventricular adrenochrome produces a drowsy state in monkeys with insensitivity to painful stimuli, as does intraventricular adrenaline; and Witt (1954) has produced abnormalities in the web-spinning of spiders by its use.

Adrenochrome is certainly highly active chemically. Meyerhof and Randall (1948) showed that it strongly inhibits the important enzymes hexokinase and phosphohexokinase concerned in the metabolism of glucose in the brain, and Abood and Romanchek (1957) have shown that it has "a formidable effect on phosphorylation processes".

Adrenochrome is so unstable and so biologically active that, if it is introduced into the blood-stream, none may survive unchanged by the time it reaches the brain.

Furthermore there is a general point concerning the relevance of the blood-levels of internally produced derivatives of adrenaline to psychosis. If noradrenaline and adrenaline are both neurohumours, mechanisms for their formation and destruction must be present close to their sites of action in the brain substance. If, therefore, the metabolism of these substances leads to the production of toxic substances, these latter can be produced locally in the brain and there give rise to symptoms resembling psychosis without having to enter the blood; or the end-product that does appear in the blood may be non-toxic. An allied argument has been presented by Shore et al. (1957a).

Clearly, much more basic work is needed on the metabolism of adrenaline both in the brain and in the rest of the body in both healthy people and schizophrenics. There is, however, some indirect evidence:

Lea (1955) argued that, since adrenochrome is an antihistamine, if schizophrenics had large amounts of circulating adrenochrome in their bodies they should be less susceptible to allergic conditions. He made a careful study of schizophrenics in British Army records, using head-injured patients as controls, and showed that there was a highly significant deficiency ($P > 0.001$) of schizophrenics with allergic conditions.

A similar finding has been published by Ehrentheil (1957), Swartz and Semrad (1951), and other workers in America. This finding also fits in with Lucy's (1954) observation that the histamine tolerance of schizophrenics is increased.

This cannot, however, be necessarily taken as evidence that adrenochrome is the responsible agent in schizophrenia, because it may merely represent an end-product of the disordered cerebral metabolism of adrenaline, and some such earlier product as the quinone derivative of adrenaline (2-methylamino-ethanol-quinone) might be the actual toxin, as described above. Rinkel et al. (1954) suggest that adrenoxine, yet another oxidative product of adrenaline, is the responsible toxin.

More recent work, however, runs against this hypothesis: Resnick et al. (1958) show that, in man, practically all the infused β-labelled adrenaline can be recovered from the urine mostly as 3-methoxy-4-hydroxy-mandelic acid.

Holland et al. (1958) measured equilibrium plasma concentrations of adrenaline and noradrenaline and detected no difference between healthy people and schizophrenics as regards the rates of utilisation of circulating adrenaline and noradrenaline.

Axelrod (1958) has been unable to detect any adrenochrome in normal or schizophrenic plasma.

Supportive evidence, however, for the hypothesis of deranged function of adrenaline in schizophrenics comes from Walaszek et al. (1958), who found that the serum of schizophrenics either abolished or reversed the systemic vasopressor response produced by the topical application of adrenaline to the exposed cerebral cortex; the serum of healthy people had no such effect. They also found that rabbit brain premedicated with the serum of schizophrenics gave significantly higher values for adrenaline and noradrenaline than did similar assays of brain tissue from rabbits pretreated with serum from healthy people.

Taraxein

The next development came from Heath's group in New Orleans. Following our suggestions about the possible role of oxidation products of adrenaline in schizophrenia, these workers supposed that the serum of schizophrenics might oxidise adrenaline faster than does the serum of healthy people. Leach and Heath (1956) confirmed this hypothesis experimentally, and Hoffer and Kenyon (1957) showed that the substance produced was adrenolutine. Heath et al. (1958) by a brilliant series of researches isolated a factor, present in the serum of schizophrenics but absent from that of healthy people, which, they reported, would reproduce clearcut symptoms of schizophrenia when injected into healthy people. They called this factor taraxein. The films showing these reactions are certainly impressive; but confirmation by an independent group is still required.

What is the chemical nature of taraxein? Heath's group also showed that blood-ceruloplasmin levels are raised in schizophrenia to such values as are found in pregnancy, chronic sepsis, and terminal carcinomatosis.

The level of blood-ceruloplasmin (measured by blood-copper) shows a positive correlation with the spontaneous remission-rate and a negative correlation with the chronicity of schizophrenia. As psychotic patients begin to improve clinically, the blood-copper level falls rapidly. So, clearly, the raising of the blood-ceruloplasmin level cannot be the cause of the schizophrenic reaction. In any case the high levels of blood-ceruloplasmin are also found in the other conditions of chronic somatic stress listed above. Hence ceruloplasmin appears to provide some protective mechanism against this stress, possibly as a method of detoxifying the excess of adrenaline produced in a severe reaction to stress.

The raised blood-ceruloplasmin of schizophrenics has been confirmed by Abood et al. (1957). There is, however, considerable overlap with normals and Ostfeld et al. (1958) showed that ceruloplasmin levels are raised by any state of emotional stress.

But the relation of taraxein to ceruloplasmin remains obscure, beyond the fact that taraxein is probably a globulin, according to S. Martens (personal communication), who has also found that adrenolutine in large doses produces a state similar to that evoked by taraxein. In animals premedication with taraxein or L.S.D. potentiates the effect of adrenolutine about tenfold. This suggests that these substances either interfere with the breakdown of adrenolutine or its binding, or sensitise the tissues to the action of adrenolutine much as L.S.D. potentiates the effect of adrenaline.

Hoagland (1957) reports important biochemical similarities between schizophrenics and healthy people who have taken L.S.D. Schizophrenics react to corticotrophin by a smaller increase than do healthy people in their excretion of 17-ketosteroids, sodium, potassium, and uric acid but by a larger increase in that of inorganic phosphate. Healthy people show similar changes after the administration of L.S.D. Hoagland therefore suggests that both L.S.D. and the toxic metabolite of schizophrenia facilitate the conjugation of inorganic phosphorus with organic substances or slow the rate of turnover of phosphorus. This suggestion is supported by the observation of Abood and Romanchek (1957) that adrenochrome has a formidable effect on phosphorylation processes. Furthermore Hoagland (1957) reports that schizophrenics do not excrete adrenaline after the administration of L.S.D. whereas healthy people do.

Second Specific Biochemical Theory

The second specific biochemical theory of schizophrenia was put forward by Woolley and Shaw (1954). This was based on the observation that L.S.D., which is the most powerful hallucinogen known, is also a potent antagonist of serotonin when tested on smooth muscle, blood-pressure, &c. Therefore Woolley and Shaw supposed that its hallucinogenic effects might be due to its interference with the action of serotonin in the brain.

Serotonin has been discovered in the brain, particularly in the phylogenetically older areas, such as the hypothalamus (Bogdanski et al. 1957, Costa and Aprison 1958). The enzyme 5-hydroxytryptophan decarboxylase, which synthesises serotonin, and monoamine oxidase, which destroys it, have also been found in the brain, also in highest concentration in the hypothalamic areas. Brodie and Shore (1957) and others have suggested that serotonin is an important chemical mediator in the nervous system. It is therefore understandable that either an excess of serotonin or a lack of it might lead to mental dysfunction. If serotonin acts by depolarisation of nerve-cells, too much of it would lead to a permanent state of depolarisation, and thus no impulses could be transmitted, and too little of it would lead again to an absence of impulses.

Other findings are also relevant to this hypothesis. An early criticism was that the brom derivative of L.S.D. (' B.O.L. 148 ') is also an antagonist of serotonin but is not hallucinogenic. Chlorpromazine is also a powerful anti-serotonin and, so far from being hallucinogenic, is powerfully antihallucinogenic. However, it is of course possible that L.S.D. and B.O.L. may have the same effect on the peripheral reactions and a different effect on the central nervous system.

A second criticism has a quantitative basis. It has been calculated that during the period of hallucinations in man there is in the brain less than 0·000001 mg. of L.S.D. per g. of brain substance (Axelrod et al. 1957), and in this very low concentration L.S.D. actually potentiates serotonin (Costa 1956). However, the possibility remains that L.S.D. produces some of its mental effects by potentiating serotonin rather than by antagonising it.

Serotonin does not produce any effects on injection but it probably crosses the blood-brain barrier only very slowly. The precursor of serotonin (5-hydroxytryptophan) can be given instead, and this readily crosses the blood-brain barrier and is transformed into serotonin in the brain and causes a great rise in the brain-serotonin level. It also causes in dogs behaviour disturbances similar to those caused by L.S.D. (Udenfriend et al. 1956.)

Bufotenin, which is chemically very closely related to serotonin and is pharmacologically almost indistinguishable from it, is a very potent hallucinogen and produces symptoms resembling psychosis. There is an important difference, however, in that 5-hydroxytryptophan produces a sleep type of electroencephalogram and L.S.D. an arousal type, indicating different methods of action of the two drugs (Costa and Rinaldi 1958). In other words, it is unlikely that they both work merely by raising the brain-serotonin level.

Another aspect of this problem has been emphasised by Costa (1956), who has found that the power of many drugs to produce symptoms resembling psychosis quantitatively parallels their power to potentiate the reaction of the cat's nictitating membrane to adrenaline. Furthermore, bufotenin has a much stronger effect than serotonin, and lysergic acid diethylamide sixty-five times the effect of B.O.L.

Another argument in favour of the serotonin hypothesis is the fact that reserpine depletes the brain of its store of serotonin (Shore et al. 1957b), and its tranquillising effect parallels in time the time course of this depletion and not the time course of the mere presence of reserpine in the brain. Reserpine actually frees serotonin from a bound form to a free form in the brain, and this free form is rapidly metabolised by amine oxidase. L.S.D. inhibits the destruction of serotonin by amine oxidase (Hoagland 1957) and thus may cause the brain-serotonin level to rise, although a rise in the level of the bound form may be necessary for the production of symptoms resembling psychosis. However, reserpine can be counteracted by giving dopamine and thus restoring the levels of catechol amines (Carlsson et al. 1957) but not by giving 5-hydroxytryptophan alone (and thus restoring the level of serotonin). The effect of these two precursors show summation if they are given together. This suggests that the effects of

reserpine are mediated both through its effects on brain serotonin and catechol amines but more strongly through the latter.

Zeller (1958) has reported a derangement of tryptophan metabolism in schizophrenia. In a tryptophan-load test schizophrenics will excrete more xanthurenic acid and less 5-hydroxyindoleacetic acid than normals. The difference was statistically significant. Serotonin is a derivative of tryptophan.

Third Specific Biochemical Theory

The third specific biochemical theory of schizophrenia implicates the metabolism of acetylcholine in the brain. Different aspects of this hypothesis have been put forward by Hoffer (1957a) and Pfeiffer and Jenney (1957). The latter argue from the facts that (1) many tranquillisers have persistent acetylcholine-like effects; (2) drugs which show the nicotinic properties of acetylcholine—e.g., di-isopropyl fluorophosphate—make schizophrenics worse; and (3) drugs which show muscarinic effects—e.g., arecoline—make them better. Therefore drugs which alter the level and activity of acetylcholine in the brain can alter the clinical state of the schizophrenic, and low levels of acetylcholine might be expected in schizophrenic brains. Administration of a precursor of acetylcholine has been reported to benefit chronic schizophrenics (Pfeiffer et al. 1957). A disorder of acetylcholine function may be secondary to an upset of adrenaline function, because adrenochrome is an anti-cholinesterase (Hoffer 1957a). One can also speculate that the metabolism of serotonin may also give rise to drugs which produce symptoms resembling psychosis, because its oxidation gives rise to a red substance chemically allied to adrenochrome.

Patzig and Block (1953) have found that injected mescaline (incorporating ^{14}C) is rapidly bound to liver protein and that, during the period (in mice) corresponding in time to the period of hallucination in man, very little mescaline was found in the brain. They suggested that this transformed mescaline was the cause of the mental symptoms, and that schizophrenia might be associated with a faulty hepatic detoxication of endogenous toxins. The absorption of the mescaline on to liver protein may block sites of detoxication of some endogenously produced toxin. Working on this hypothesis Harley-Mason et al. (1957) looked for metabolites either of mescaline or of abnormal bodily metabolism in the urine of healthy volunteers who had taken mescaline. A new metabolite of mescaline (3 methoxy, 4–5 dihydroxyphenylacetic acid) was discovered but was thought unlikely to cause mescaline psychosis.

Conclusion

The general concept of schizophrenia that arises from the facts at present at our disposal is that it is a genetically determined disorder of the metabolism of the neurohumours of the central nervous system—noradrenaline and adrenaline, serotonin and/or acetylcholine. The cause of schizophrenia may be a primary genetically determined fault in one of these systems—e.g., the production of toxic oxidative metabolites of adrenaline, which would disrupt the normal functions of the brain through their actions on key enzyme systems, such as hexokinase and phosphorylation mechanisms, as well as their actions on the metabolism of the other neurohumours, such as the action of adrenochrome on cholinesterase. On the other hand, the different clinical pictures of schizophrenia may result from different genetically determined faults in more than one of these systems, producing, through the interaction of these systems, allied clinical pictures.

There remain two advantages of the concept of the primary fault in the metabolism of adrenaline. The clinical course of schizophrenia strongly suggests by its indolent chronicity the operation of a vicious circle. The adrenaline-derivative hypothesis offers the possibility of two such vicious circles (see below); it also offers an explanation of the clinical correlation of the disease with stress of some kind.

It is well recognised that the onset of schizophrenia is commonly linked to some specific stress, perhaps a battle stress, or emotional, interpersonal, or biological stress. Such stress situations will be associated with a chronic overactivity of the sympathetic system, and it is to be expected that any latent faults in this system would become apparent at this time.

This is where the first vicious circle comes in. The production, by the metabolism of adrenaline, of end-products which cause symptoms resembling psychosis will lead to further stress because the experience of the effects of these end-products is also stressful, as anyone who has experienced the appalling effects of mescaline and sympathetic overactivity combined, as I have, can testify. This further stress will lead to the production of further activity in the sympathetic nervous system and thus more adrenaline, more toxic breakdown products of this adrenaline, and so, in turn, more stress, thus constituting the vicious circle.

The second possible vicious circle is constituted by the anti-cholinesterase effect of adrenochrome (Hoffer 1957a). The raised level of activity of the sympathetic ganglia (which are cholinergic) thereby occasioned will lead to an increased output of adrenaline and so of the toxins which may be responsible for schizophrenia.

A further advantage of the theory that metabolic products of adrenaline are responsible for schizophrenia is that it enables us to explain quite simply the role of psychological factors in schizophrenia. One may postulate two factors: (1) a genetic predisposition which may be stronger in some people than others; and (2) different patterns of emotional experience that, lasting for a sufficient time, may give rise to different patterns of biochemical activity in the vastly complex and variegated anatomical and biochemical mechanisms that underlie the experience, coordination, and expression of emotions, attitudes, dreams, wishes, unconscious desires, &c. Some of these patterns may be more susceptible than others to the action of the toxins which produce schizophrenia. Some may even produce such toxins or function at a degree of neurohumoral imbalance in the mechanisms sufficient to cause aberrant behaviour typical of schizophrenia. One should not underestimate the biochemical and electrical storms that must sweep through the brain in the advent of powerful emotions. The extreme range of symptoms and the variety of individual responses to L.S.D. and mescaline again suggest that there are great individual biochemical differences in the higher mental functions.

A final advantage of our hypothesis is that there are already well-known metabolic diseases due to abnormalities in the metabolism of tyrosine (adrenaline is a derivative of tyrosine): phenylpyruvic oligophrenia, alkaptonuria, albinism, and tyrosinosis.

In view of all this evidence it is safe to conclude that there are now enough facts to show that purely psycho-

genic theories of the causation of schizophrenia along psychodynamic lines can no longer be held as total explanations of the causation of schizophrenia. Their place should be in a presentation of contributory factors, as indeed are the biochemical factors I have been discussing.

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Congress

DIABETES

THE third congress of the International Diabetes Federation was held in Düsseldorf from July 21 to 25, under the joint presidency of Prof. J. P. HOET (Louvain) and Prof. K. OBERDISSE (Düsseldorf). The congress received a telegram of welcome from Dr. Adenauer; and honorary degrees were awarded to Dr. E. P. Joslin and (in his absence) to Prof. B. A. Houssay.

In his Banting memorial lecture Prof. G. KATSCH (Greifswald) spoke on Conditions for Conditioned Health. He gave a comprehensive review of the social aspects of diabetes and repeated the advice to diabetics which is inscribed on the walls of his own clinic—"courage, moderation, and activity".

The congress sessions were divided into lay and scientific, and usually one lay and two scientific sessions were in progress simultaneously. Virtually every aspect of diabetes was discussed, most time being devoted to the oral antidiabetic compounds, largely exploited since the Cambridge congress three years ago, and to various aspects of diabetic angiopathy, which is a problem of growing importance.

Action of Insulin

The discussion of the action of insulin left the subject more open than it had been three years previously. There is now no agreement about the importance or otherwise of insulin's action on the liver, especially in view of the negative results of Ashmore, Cahill, Earle, and Zottu on the effect of insulin on glucose production by the liver measured directly in experimental animals.

Prof. C. DE DUVE (Louvain) still believed, however, that insulin affected hepatic gluconeogenesis primarily and not secondarily. The evidence for the permeability hypothesis of insulin's action was well stated by Dr. R. LEVINE (Chicago) and Dr. C. R. PARK (Nashville). Dr. Park believed that glucose permeates the cell by an enzymic process, and Dr. B. L. HORECKER (Paris) drew some interesting analogies with enzymic blocks of sugar permeases in mutants of *Escherichia coli*. Dr. P. J. RANDLE (Cambridge) suggested that insulin permits glucose to enter the cell by inhibiting the role of energy-rich phosphate bonds in establishing the barrier to glucose on the cell surface. Anoxia or salicylates seem to encourage the permeation of glucose by a direct inhibition of oxidative phosphorylation.

Dr. D. B. MARTIN (Boston) described the immediate direct action of insulin on adipose tissue in contrast to the apparently delayed effect of insulin on liver. Prof. C. N. H. LONG (New Haven) indicated that the effects of the adrenal glucocorticoids on the liver were independent of insulin, and referred to steroid diabetes as an overflow diabetes, the excess glucose coming from increased gluconeogenesis in the liver and a partial block of glucose utilisation in the muscles.

Insulin Assay

Some of the reasons were discussed for the different serum values obtained by slightly differing techniques based on the isolated rat diaphragm. Dr. H. v. d. GELD (Amsterdam) considered that small amounts of adrenaline significantly opposed the action of insulin by reducing glucose uptake by the diaphragm, and there was general agreement that higher absolute values of insulin activity were obtained if dilute rather than whole serum was used. It was suggested that results of different workers would be more comparable if a 1-in-10 dilution of serum was used, and that the results should be expressed as units of insulin activity per litre of serum.

Dr. MARTIN described the advantages of the insulin assay using rat adipose tissue and ^{14}C glucose. The sensitivity of the method is similar to that employing rat diaphragm, as described by Dr. J. VALLANCE-OWEN (London) and Dr. P. H. WRIGHT (London). Insulin activity can be shown to be associated with the serum-proteins, mainly the β-globulins according to the Amsterdam group, or the electro-

phoretically slow-moving albumin according to Dr. K. W. TAYLOR and Dr. RANDLE (Cambridge).

Various insulin inhibitors have been recognised in serum. These include insulin antibodies in the inter-γ-β-globulin zone, the lipoproteins in alloxan-diabetic rats, and fractions in the serum of depancreatised cats, dependent on intact adrenal and pituitary glands, as were described by Dr. R. H. WILLIAMS (Seattle). Dr. J. B. FIELD (Bethesda) has found an additional insulin antagonist, migrating electrophoretically with the α_1 globulins of patients in diabetic ketosis. Dr. W. OAKLEY (London) described the dramatic effect of prednisone in reducing insulin resistance in certain types of diabetes, which he has been studying.

Diabetic Angiopathy

Dr. D. ADLERSBERG (New York) emphasised the ætiological role of raised serum-triglyceride levels, and Prof. P. A. BASTENIE (Brussels) drew attention to the high rate of excretion of adrenal 11-oxysteroids in such patients. Prof. M. BÜRGER (Leipzig) considered that insulin lack directly affected the capillaries and thus the blood-pressure and eventually the electrocardiographic findings. Dr. H. T. RICKETTS (Chicago) hoped to exclude genetic factors by working with dogs with experimental diabetes of long duration. The role of poor diabetic control in promoting angiopathy was clear but less important than simple ageing. Prof. K. LUNDBAEK (Aarhus) described the long-term development of diabetic vascular disease in the human, and suggested that it was the cause of other late complications, such as rubeosis iridis diabetica, diabetic osteopathy, the " stiff hands syndrome ", and multiple areolar exudates of the retina. Little helpful information regarding the treatment of angiopathy was forthcoming apart from the desirability of good diabetic control.

Discussing diabetic nephropathy, Dr. H. F. ROOT (Boston) emphasised its increasing importance as a cause of death in early-onset diabetics, but he believed that optimal control could postpone or prevent its development. Dr. J. F. HARTMANN (Minneapolis), on the other hand, using electron microscopy of renal biopsies, had found evidence of renal involvement as early as five months from the clinical onset of diabetes. Dr. A. GOTH (Budapest) produced renal lesions in rats by causing wide variations in the blood-sugar with insulin alternating with glucose by stomach tube. Prof. P. KIMMELSTIEL (Milwaukee) showed a series of beautiful slides illustrating the diabetic kidney condition named after himself and Prof. CLIFFORD WILSON (London). The stages of diabetic retinopathy were also well illustrated by Dr. R. THIEL (Frankfurt). Dr. T. YOSHIDA (Osaka) claimed that calcium pantothenate in association with good diabetic control effectively relieved the symptoms of diabetic neuropathy.

Intermediary Metabolism in Diabetes

Dr. O. WIELAND (Munich) drew attention to the probable competition between the metabolites of fat and carbohydrate for the available coenzyme A, which was concerned with acetylation processes. Dr. I. KELSEY FRY (London) had studied the changes in blood-pyruvate levels during glucose and glucose and insulin loads in normal subjects and diabetics. Only " brittle " diabetics showed a consistent pattern with high fasting pyruvate levels, unaffected by glucose but increasing sharply after insulin and glucose. He suggested that diabetics had a metabolic block at the level of pyruvic-acid-oxidase, and integrated this suggestion with the effect of dimercaprol (BAL) in reducing blood-pyruvate and glucose levels in such diabetics.

Diabetes and Pregnancy

Dr. A. HAGEN (Gentofte, Denmark) performed a useful service in establishing the blood-sugar values of normal and prediabetic women during pregnancy. Dr. J. J. HOET described experience in his father's clinic in Louvain, which specialises in the study of prediabetic pathological pregnancies. Dr. Hoet indicated his faith in the beneficial effect of insulin, even in prediabetic pregnancies, and of thyroid when indicated. The infant mortality of diabetic pregnancies can be most effectively reduced by strict diabeic control, as was illustrated by the findings of Dr. J. M. MALINS (Birmingham). With improved survival-rates the incidence of congenital anomalies in the babies would assume increasing importance, and Dr. R. G. PALEY (Leeds) reported studies on this aspect.

Dr. M. OSLER (Copenhagen) measured the total body-water and extracellular water in the newborn infants of normal and of diabetic mothers. The infants of diabetic mothers contained significantly less water, presumably because their body contained relatively more fat and glycogen than that of infants of normal mothers. Dr. R. BOULIN (Paris) made the interesting point that diabetic mothers have nearly three times the tendency of diabetic fathers to hand down the diabetes to their children.

Oral Antidiabetic Drugs

Much of the discussion of the oral antidiabetic compounds centred on the mechanism of the hypoglycæmic action of the sulphonylureas. Prof. A. LOUBATIÈRES (Montpellier) felt confident that these compounds stimulated the release of insulin and later the hyperplasia of the β cells of the islets of Langerhans, but his work was based on experimental animals, not man. Investigators of human diabetes, such as Dr. T. MUNKNER (Copenhagen), had shown that tolbutamide reduced the hepatic glucose output without changing the hepatic or limb blood-flow or affecting the arteriovenous blood-sugar difference in the leg. Prof. J. D. ACHELIS (Mannheim-Waldhof) agreed that some of the drug's action in humans is extrapancreatic. Prof. C. V. HOLT (Hamburg) attributed the main hypoglycæmic action in man to a stimulation of endogenous insulin secretion, and other investigators brought forward evidence to support this view. Thus, Dr. E. F. PFEIFFER (Boston) found a greater increase in the insulin activity of the portal venous blood of animals receiving sulphonylureas than that of the femoral venous blood. This raised the question whether insulin in the portal venous circulation had a different effect from insulin in the systemic circulation. Dr. L. L. MADISON (Dallas) had evidence to support this suggestion. Thus in dogs the slow administration of insulin into the portal vein produced as much hypoglycæmia as a peripheral injection, but with much less effect on the arteriovenous blood-sugar differences. Moreover, the hepatic binding of ^{131}I-labelled insulin was significantly greater when it was given into the portal vein than when it was injected systemically. Prof. W. J. H. BUTTERFIELD (London) and Dr. O. J. RAFAELSON (Aarhus) confirmed that the sulphonylureas increased the uptake of glucose in the muscles of the intact human and of the isolated rat diaphragm respectively. This could be explained by an insulin-like action, although it did not constitute a proof. Further confirmation was provided by Prof. RUSSELL FRASER and his colleagues (London), for they found in a blind trial that tolbutamide would raise the plasma-insulin activity only in those diabetics who responded satisfactorily to the hypoglycæmic action of tolbutamide. It would thus appear that the relatively great effect of the hypoglycæmic sulphonylureas on the liver as compared with on the muscles (Dr. V. CONARD, Brussels) might be explicable if endogenous insulin was released and had its main effect on the liver.

Many studies were reported of the comparative toxicity and efficacy of carbutamide, tolbutamide, and the new sulphonylurea, chlorpropamide. European workers have not found cause to avoid carbutamide as studiously as their American colleagues, who were alarmed by early reports of bone-marrow depression. Luckily the serious effects of tolbutamide on the liver of dogs have not been noted in man or indeed in other experimental animals. There has been an increasing tendency to use carbutamide only in small doses (Dr. R. BOULIN, Paris) or in intermittent courses (Dr. I. MURRAY, Glasgow). The toxicity of tolbutamide was less than that of carbutamide (Dr. F. BERTRAM, Hamburg; Dr. A. MARBLE, Boston), but neither compound was as potent a hypoglycæmic agent as chlorpropamide, which needed to be given in a dose of only 200–500 mg. per day to maintain its effect. The long-term toxicity of chlorpropamide has still to be established, but it is already apparent that doses comparable to those used for tolbutamide are certainly toxic (Prof. H. A. HEINSON, Zeven; Dr. JOAN WALKER, Leicester).

Much information was also presented about the hypo-

glycæmic effect and toxicity of another oral antidiabetic compound, phenylethylbiguanide (D.B.I.) and its analogues. Such compounds inhibit certain oxidative enzymes (Dr. R. H. WILLIAMS, Seattle) and increase the glucose uptake even of depancreatised animals or of juvenile diabetics. Hepatic gluconeogenesis is sharply depressed, and doses of more than 100–200 mg. per day produce a high incidence of toxic effects, such as anorexia, nausea, vomiting, diarrhœa, weakness, or a metallic taste in the mouth. Dr. P. WHITE (Boston) has shown that D.B.I. can reduce the insulin requirement of juvenile diabetics and be used alone in a few of them. Such synergism between different hypoglycæmic agents was illustrated in a case of insulin-resistant diabetes by Dr. N. BILHAN (Istanbul), using tolbutamide with insulin, and by the use of salicylates with sulphonylureas by Dr. J. M. STOWERS (Dundee).

A New Insulin

Dr. J. SCHLICHTKRULL, of the Novo Laboratories, Copenhagen, described a new insulin, which may be an improvement on the lente series. No zinc is added to the insulin crystals, and a quicker initial action than that of lente insulin is obtained by including a proportion of pig insulin in a mixture with slower acting beef insulin, prepared in the same way.

Detection of Diabetes

The lay sessions of the congress made progress in establishing the need for and methods of diabetes detection drives. A committee representing 14 countries was formed and hopes to work in association with the World Health Organisation. Dr. M. NAKAYAMA's detection drive among people over 40 years of age in Tokyo revealed 3·1% of previously unknown diabetics and another 3·3% of suspected diabetics. Dr. J. J. A. REID (Dundee) discussed the results of his personal survey of employment problems among diabetics, and Mr. J. G. L. JACKSON (London) reported on the results of a questionnaire about employment sent to the 22,000 members of the British Diabetic Association. The expense of diabetic diets and insulin is still a problem in many parts of the world. Dr. W. TROUP (Ottawa) described the increasingly progressive attitude of insurance companies to the life assurance of diabetics.

Parliament

Commemoration Day

WHEN the National Health Service was started ten years ago Mr. ANEURIN BEVAN was Minister of Health, and on July 30 he appropriately opened the debate held in the House of Commons to mark its tenth anniversary. Behind the service, he said, lay two principles—the provision of a comprehensive, free, health service for all the people of the country in time of need, and the redistribution of the national income by a special method of financing the service. On the whole he thought that the first principle had been achieved and that there was general, though not uncritical, satisfaction with the therapeutic side of the service.

About the financial side he confessed that he was getting a little worried. When the service was being planned, he had rejected the method of insurance as inapplicable to a scheme of this kind and had decided that the fairest way to finance the service was from Exchequer funds by general taxation. As the Treasury was to carry the full cost of the service, it claimed the portion of the National Health Insurance contribution which had formerly been used for medical benefits. This was reasonable enough, but, Mr. Bevan stressed, it was an appropriation-in-aid taken from the Insurance Fund by the Treasury, and there was no organic, financial, or administrative link between National Insurance and the National Health Service. By assuming this link, the Government, instead of increasing taxation to find additional money for the service, had called for the money from the National Insurance Fund by a poll tax. This was an unjustified transfer of the burden from the well-to-do to the poorest.

One of the difficulties of the service had been the number of Ministers. They had followed one after the other, to their mutual embarrassment and to the dismay of the nation. By the time that they had acquired a jealousy for their position and a knowledge of it, they were sent away. They had not enough time in office to acquire sufficient stature to be able to stand against the importunities of the Treasury.

Mr. Bevan had always regarded pay-beds as one of the concessions which had to be made to the pressures of the moment when the service was started. He was distressed to learn that this concession was sometimes abused. He would not say for a single moment that the practice of allowing a paying patient to jump the hospital waiting-list was universal, but it had amounted to so grave an abuse as to impair the service.

When people talked about the cost of the service he hoped that they would take into account that the service had a secret silent column which never appeared in the balance sheet. It comprised the enormous number of people who were back at work and who would not be there without its help.

Mr. DEREK WALKER-SMITH, the Minister of Health, thought that ten years had been long enough to establish some sound record of performance, but was yet short enough to make it appropriate to concentrate on the future rather than the past. Two signposts for future action were, he suggested, provided by our success with tuberculosis and diphtheria. It showed the importance and potential of preventive medicine and the possibility of solving the accommodation problem of our hospitals by eliminating some diseases. Two of our gravest problems—the care of the aged and of the mentally ill—had a common denominator. In both we sought a shift of emphasis to outpatient treatment and care within the community. Only in this way could we hope to have a service adequate to the needs of the patients without creating a burden too great for our resources to bear.

But whatever success we achieved in this policy, there would always be an important residue of patients who would need care in hospital. At present the running cost of hospitals took nearly 54% of our total expenditure on the health service. Where so much money was being spent we must seek the highest common factor of efficiency and economy in administration. The Ministry's experimental organisation and methods service had already shown that we could best ensure economy by critical and detailed analysis of hospital work on the spot. Particularly in manual work large savings of time could sometimes be made, and these potential savings were a hidden reserve which could be used to offset the recent reduction in working hours and to relieve our nurses of extraneous tasks. The present experimental O. and M. unit was to be enlarged and made permanent under a full-time assistant secretary by the Ministry. He was also considering a suggestion by the Royal College of Nursing that an advisory council on work study should be set up.

The country had made a very considerable investment in health, and he thought that with the years we should see an increasing return. The return we needed was not only better treatment and improved prospects of cure, but the prevention and where possible the elimination of disease, resulting in a positive improvement in health which would be reflected "in the factory, the foundry, and the farm, and not merely in the convalescent home".

Dr. A. D. D. BROUGHTON believed that one of the most serious problems of the service was the overcrowding in the mental hospitals, yet he asked the Minister to resist proposals to build new hospitals to relieve congestion. Dr. Broughton was sure that wherever possible the patients should remain in familiar surroundings and if possible at work.

Mr. ROBERT COOKE thought that the craving for new apparatus should also be resisted. These things quickly went out of date and this could lead to work. Clearly the best facilities should be available, but not necessarily in every hospital.

Sir FREDERICK MESSER believed that more money should be spent on keeping patients out of hospital. He would like to see

the executive committee become a more effective administrative unit; with closer liaison between general practitioners and the local health authority, the domiciliary services could usefully be extended. One of the inconsistencies of the N.H.S. was that a patient usually had to pay for a home help, yet he was not asked for any contribution towards the wages of the wardmaid. Stronger incentives for a more efficient domiciliary service would, in his view, be better for the patient and cheaper for the taxpayer.

Mr. KENNETH ROBINSON was disturbed by the steady drift from whole-time to part-time consultants. He, too, thought that some part-time consultants were abusing the pay-bed facilities of the hospital. But the main thing about consultants was that we had not nearly enough of them. In some areas and in some specialties we needed many more. All over the country senior registrars and even registrars were doing work which should be done by consultants. What was even more disturbing was that the quality of the registrars coming forward was beginning to deteriorate. The worry and frustration among registrars had acted as a powerful disincentive to medical graduates to make their way on to the consultants' ladder.

Mr. ARTHUR BLENKINSOP was dismayed by the calm assumption that we were wasting enormous sums on the service when in fact the total expenditure was by no means so terrifyingly great in real terms. People were terrified because for the first time they were seeing the total expenditure on medical care expressed in money. Our expenditure per head by the population was no greater than that of other countries, and much less than that of the United States. He regretted a lack of leadership in the Ministry and among the professions concerned with the service. As a result, a great deal of the time of highly intelligent and well-trained people was spent on all kinds of professional squabbles which would not be necessary if there were a greater sense of what kind of service we were trying to build and what were the main problems we were trying to solve. For instance, we did not seem to appreciate the urgency and importance of industrial health. It should be the natural job of practitioners working in groups and linked with industry, as at Harlow and Slough. Again, the present local-authority services were very haphazard; yet if we were to cope with an ageing population, they should be given priority. Yet by introducing the block-grant procedure, the Government would make it much more difficult for the local authorities to expand their health services. What, for instance, was the good of decertifying patients if the local authorities were unable to provide residential accommodation for them?

Mr. JOHN CRONIN, F.R.C.S., said that though the profession had cooperated in the N.H.S. in an able and honourable way, few doctors had any idea of the economics of the service, and none of them by its administrative framework had any incentive towards reasonable economy even in the best interest of the patient. He believed that the service would gain from a mild and general economic supervision of doctors, as doctors, by doctors.

Dr. EDITH SUMMERSKILL also thought that the Minister should reconsider fundamentals, and suggested that the capitation system was not calculated to improve the quality of the service. For some people it only served as an incentive to achieve the maximum list of patients and encouraged acquiescent prescribing. Again was it economical for us to have part-time rather than whole-time consultants? The payment of a consultant by sessions might encourage him to keep his outpatient department fully occupied and his beds full.

Mr. RICHARD THOMPSON, parliamentary secretary to the Ministry, agreed that the local-authority community care services should be enlarged. The Government had made it clear that they did not consider that the introduction of the general grant would hinder this. The local authorities' associations had, however, suggested that it would be preferable that special financial provision should be made for these services and their views were being very carefully considered.

Turning to the future he said that our general aim must clearly be to keep those not in actual need of hospital care and treatment out of hospital and in the community for as long as possible. Of all our public services the N.H.S. probably depended most on voluntary help for its administration, and we must be grateful to the members of hospital boards and committees for their work in this worthwhile project. "It is in this spirit of cooperation and dedication to a great cause that we can face the future with confidence."

Artificial Insemination

The Earl of FEVERSHAM has agreed to serve as chairman of the proposed departmental committee on artificial insemination. The committee's terms of reference are:

To inquire into the existing practice of human artificial insemination and its legal consequences and to consider whether, taking account of the interests of individuals involved and of society as a whole, any change in the law is necessary or desirable.

Royal Assent

Bills which received the Royal Assent before the end of the session included the Medical Act, 1956 (Amendment) Bill and the Children Bill.

QUESTION TIME

Charing Cross Hospital

Mr. A. G. F. RIPPON asked the Minister of Health whether he had reached a decision regarding the future of Charing Cross Hospital.—Mr. DEREK WALKER-SMITH replied: On Feb. 9, 1955, the House was informed by the then Minister that the Government's plans for hospital building expected to start in the next few years included a project for the rebuilding of Charing Cross Hospital at Northwick Park, Harrow. This proposal has had to be abandoned because further consideration by the University of London and the University Grants Committee caused these bodies to decide that it was not in the best interests of medical education to remove the Charing Cross Hospital Medical School to Northwick Park.

The existing Charing Cross Hospital building is outmoded and inadequate for hospital purposes, and it cannot be properly redeveloped on the same site. To meet University requirements, the new site must be within reasonable access of all the facilities of the University, including the basic sciences and general student activities, and in August last the responsible hospital authorities were asked to consider the possibility of rebuilding on the site of the existing Fulham Hospital, which is in close proximity to these University facilities and which also requires rebuilding. I am glad to say that a large measure of agreement has been reached by the responsible hospital authorities about the practicability of amalgamating Charing Cross Hospital, the West London Hospital, the Fulham Hospital, and the Fulham Maternity Hospital, as a first step towards the ultimate replacement of all of them by a new general teaching hospital at Fulham.

I have given close and careful consideration to all the representations made to me, including those made by the committee headed by the Mayor of Fulham, and I am satisfied that the Board of Governors of Charing Cross Hospital, in close cooperation with the South West Metropolitan Regional Hospital Board, will provide a service to the locality which will compare favourably with that which might have been provided by the rebuilding of Fulham Hospital as a non-teaching hospital.

I propose, therefore, to make arrangements for the proposed regrouping at the earliest practicable date so that the replanning of the new teaching hospital may proceed without delay. The necessary facilities for clinical teaching will be provided at the new hospital, but the question of preclinical facilities is under consideration in consultation with the University and the University Grants Committee.

Institute of Criminology

Mr. H. M. HYDE asked the Home Secretary to make a statement on the official proposal for an institute of criminology.

Mr. R. A. BUTLER replied: Discussions have been pro-

ceeding with university authorities and I am also consulting the University Grants Committee. I have now been informed by the Vice-Chancellor of Cambridge University that, provided the necessary funds can be made available, the university will be glad to consider the establishment of an institute of criminology, whose functions would include both teaching and research, as well as facilities for exchange of views and information with those concerned with the practical administration of the law. The nucleus of the institute would be the existing department of criminal science, but it would be developed on a broader basis and steps would be taken to associate all interested faculties with its management. I have told the Vice-Chancellor that I warmly welcome this proposal and that I am confident that its fulfilment would make an indispensable contribution to the study of the problems of crime and the treatment of offenders.

Family Planning

Mrs. LENA JEGER asked the Minister what were the present facilities within the National Health Service for family planning advice and treatment; and why he did not propose to encourage a widening of existing facilities.—Mr. WALKER-SMITH replied: The present facilities are for advice and treatment where pregnancy would be detrimental to health. Help is also given in some areas to voluntary associations by making premises available. I do not consider that there is a sufficient case in present circumstances for seeking to widen these facilities.

New Hospitals

Since 1948, under the National Health Service in Great Britain 1 new hospital has been completed. 3 others are in part use, and 8 are under construction.

Public Health

Sickness Benefit

THE biggest influenza epidemic since the National Insurance scheme began brought new claims for sickness benefit in 1957 up to the record figure of 9½ million. According to the report of the Ministry of Pensions and National Insurance for 1957 which has just been published,[1] 5 million claims (twice the average for the season) were received between late August and the end of the year, suggesting that 1 in 8 of the 20 million people insured for sickness benefit may have had influenza. The peak was reached in the first week of October, when 567,000 claims came in—130,000 more than the highest week's figure in the epidemic of 1951. The epidemic is estimated to have cost the National Insurance Fund £10 million.

1. Cmd. 493. H.M. Stationery Office. 8*s*.

Infectious Diseases in England and Wales

Disease	Week ended July			
	5	12	19	26*
Diphtheria	3	..	3	..
Dysentery	919	741	712	637
Encephalitis:				
Infective	4	4	1	5
Post-infectious	2	1	5	8
Food-poisoning	342	228	332	486
Measles, excluding rubella	6442	7078	6674	6594
Meningococcal infection	21	15	15	16
Ophthalmia neonatorum	17	12	23	15
Paratyphoid fever	4	4	4	11
Pneumonia, primary or influenzal	232	220	220	182
Poliomyelitis:				
Paralytic	30	35	37	38
Non-paralytic	18	24	20	25
Puerperal pyrexia	183	229	223	188
Scarlet fever	665	625	651	672
Smallpox	..	..	..	..
Tuberculosis:				
Respiratory	535	497	578	521
Meninges and C.N.S.	4	12	8	6
Other	56	58	73	67
Typhoid fever	1	18	4	..
Whooping-cough	882	816	827	749

* Not including late returns.

Special Articles

Medical Staffing of Hospitals

THE Joint Working Party on Medical Staffing of Hospitals has elected Prof. Robert Platt, P.R.C.P., as its chairman.

This working party was appointed by the Minister of Health, the Secretary of State for Scotland, and the Joint Consultants Committee to study, in the light of experience of the hospital service since 1948 and of all other relevant considerations, the principles on which the medical staffing structure in the hospital service should be organised.

The working party is inviting regional hospital boards, professional organisations including organisations of specialists and the associations of hospital authorities, to submit statements of evidence. Any other body or person desiring to submit evidence should notify one of the joint secretaries before the end of October. The joint secretaries are Mr. N. C. Rowland of the Ministry of Health and Dr. D. P. Stevenson of the British Medical Association.

Medicine and the Law

Duty to Disclose Epilepsy

A PERSON who suffers from epileptic fits is not under any general duty to disclose the fact, but the law recognises that there are circumstances in which he ought to do so.

A few years ago a workman took employment as a painter without informing his employers that he was subject to epileptic fits and had been warned by his doctor not to work at heights. While working on a platform about 20 feet above ground he had a fit, fell to the ground, and was killed. The platform did not conform to statutory regulations and had it been properly protected the man might not have fallen to the ground. The court held that the two parties were equally at fault, with the result that the damages payable to the widow by the employers were reduced by half.[1]

Even more compelling is the duty of an epileptic who is contemplating marriage. Failure to disclose the facts to the intended spouse may later result in the marriage being nullified. A decree of nullity under section 8 of the Matrimonial Causes Act, 1950, has been granted to a woman who married in ignorance of the fact that her husband suffered from epileptic fits.[2] At the time of the wedding the man was 21, the bride 18. The man had the first attack three months before the wedding when discussing the arrangements with her. He did not have hospital treatment as his doctor, who diagnosed an epileptic fit, advised. He had a similar attack on the occasion of the wedding ceremony before the bride had got to the church; she was not informed of it although the ceremony was late.

Although the man had lodged at the home of the girl's parents before the wedding, the judge was satisfied that she was entirely ignorant of his condition until after she left him.

Section 8 of the Matrimonial Causes Act, 1950, provides that recurrent attacks of epilepsy are sufficient ground for a decree of nullity provided three conditions are satisfied. The petitioner must be ignorant of the fact at the time of the marriage, proceedings must be instituted within a year of the marriage, and marital intercourse must not have taken place with the petitioner's consent after discovery of the fact.

1. Cork *v.* Kirby Maclean (1952).
2. *Daily Telegraph*, July 23, 1958.

In England Now

A Running Commentary by Peripatetic Correspondents

NOT being an efficient G.P.—that is, not having a secretary—I'm constantly facing the problem of remembering my patients' names. When one enters my surgery I often find myself saying (to myself, of course) "Ah! here comes 193-Copthorne-Avenue, or 61-Huntscliff-Common." Then aloud, diffidently and apologetically—"Er, I'm afraid I've forgotten your name."

Not so with the Brown family. I know them all very well. Mr. Brown, now resting in peace, I saw every month for all the eight years I had been in practice. He needed dressings for his eczema. Then I saw him almost daily for many many weeks while he was under my care in the local G.P. hospital and during his final long illness at home. Mrs. Brown, too, I have greeted many times during my repeated cures of her leg ulcers—the relapses, that is. Then there's Mr. Brown's sister, who had a very severe ophthalmic herpes, and there's unmarried daughter Joan—I.Q. not very high and definitely odd. The son, Eddie, has 37 attendances recorded during the past eight years, strangely enough without there ever having been noted a firm diagnosis (should it be inadequate personality or perhaps inadequate family doctor?). So when a Brown comes into my surgery I don't say to myself, "Ah! here comes 34-Acacia-Drive," I say "Here's Eddie Brown" or "Here's Joan Brown."

But I hadn't seen any of the family for three or four weeks, when a note came through my door. "Would you please come to see Mrs. Brown. She has been at M—— for a few days and has had a stroke. She will be home at 5 o'clock." At 5.15 sharp I am at 34, Acacia Drive. "Hello, Mrs. Brown, what's happened?" I asked. "Didn't the doctor at M—— telephone you?" she said. "No," I replied, "not yet." "Well," said Mrs. Brown, "I expect he's had some difficulty in finding your number. None of us could remember your name."

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The heart bleeds for your correspondent of last week beneath whom plastic seats are continually crumbling. Such a long tale of disintegration must surely have a cause and he had better take a careful look at his profile in a full-length mirror, or better still ask for the candid comments of his wife who will be more objective. There comes a time when the odd stones come on us with a rush: $13^1/_2$ is easily confused with $14^1/_2$, and pretty soon it will be $15^1/_2$, but by then the earlier figures have been forgotten and one goes about in the fond fiction that it was $15^1/_2$ all along. This is known as "repression of an intolerable memory" (Freud) and operates also on paunches, chins, bags under the eyes, and receding hair: one cannot recall the time when these things weren't. It also explains why old photograph albums get so easily misplaced.

Insight comes slowly, and it is always easier to spot increasing disproportion in others: realisation came ultimately to me, not through shattered seats, but tennis. My service matured with increasing years and gained in power and reliability, as did my ground strokes: middle-aged guile enhanced my skill and things were pretty good until I attempted the overhead smash. Lobs which I used to "jump to" and catch squarely in the middle of the racket started to get lost in the short strings at the end, and this year hit the wood. Next year I shall miss altogether. It could be argued that people are lobbing higher these days, but I *know*. It is all a question of power/weight ratio.

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I had no particular reason to question the mode of arrival and departure of the night sisters until one night after a party, when I happened to be on duty late, I came across a door which I had not noticed before. I opened it and peeped in. The room was bare except for a line of hooks on which hung in a neat row seven long cloaks; six were a dark green; the seventh was jet black. On each cloak rested a high-pointed black cap; beside each cloak, propped against the wall, was a tall broom; on the ground beside each broom a huge black cat snoozed. This sight aroused my suspicions.

The next morning before dawn I hid myself near the front door hoping either to confirm or disprove my suspicions. I hardly dared to breathe as the first sister appeared at the end of the corridor, came nearer, and walked past me. She had changed out of uniform, wore a heavy overcoat, and carried a large bag. I wondered what was in the bag. She reached the front door, stood still for a second gazing about her, as though sensing that all was not quite as usual, opened the door and walked off down the drive. Each sister left in turn; and last of all the night superintendent, whose bag was a size larger than the others, came into sight, and stood by the front door for a second before leaving. I craned desperately from my hiding-place, and caught a glimpse of some jet-black cloth protruding from her bag. This last effort, however, proved my undoing: I fell forwards on my face in the middle of the corridor. The night superintendent looked back. "Good morning, doctor," she said. I thought she said it rather spitefully. I felt a little chastened, as she too departed down the drive.

I suppose it is not for mortal eyes to see *exactly* how the night sisters come and go.

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Mrs. X-Y was reluctant to send her baby to hospital. However, I told her that her baby would be nursed by a specially picked staff in a special ward in a very good hospital and she gave her consent—influenced, I think, by the fact that I had had two babies myself.

A few days later I went to the children's ward to see the baby and found her in the arms of a nurse who was trying to get her to sleep. Apart from being very cross, my patient was doing well. Sister was off duty, so the nurse and I walked up and down the ward for a time and I thought the baby was going to settle down. But we happened to stop at the window and we discovered two buxom young women digging the hospital garden, and that seemed to make the baby crosser than ever. The young lady gardeners were making a poor job of it and I was tempted to take the baby myself and send the nurse down to give them a hand. He was a tough, muscular young fellow and would have finished the plot for them in no time, but I thought the head gardener might not like it. So I left him rocking the baby, first on one arm and then on the other, and went on to report to Mrs. X-Y. I told her that it would have been difficult to find a better nurse.

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At lunch, the physicist was being sarcastic over clinicians using apparatus which they did not understand. The only surgeon present rose at once to this bait and said that he would never dream of using anything which he did not thoroughly understand. "Do you use diathermy?" asked the physicist. "Of course," was the reply. "Very well then, I will bet you sixpence that you cannot answer two out of four elementary questions about it." The surgeon looked rather shaken by this but had to agree. These were the questions:

(1) What type of current is used—e.g., A.C., D.C., or interrupted? What is the approximate voltage and amperage?

(2) What happens when you switch over from "cutting" to "coagulating"?

(3) In what concentration of saline should the pad enclosing the indifferent electrode be soaked?

(4) How can a patient get burnt in areas remote from both the active and the indifferent electrode?

The surgeon's score was . . . no, my gallstone still bothers me and I think that he already suspects me of being a peripat.

• • •

This year the Widdicombe Agricultural Show shows another loss. The committee are thinking of including classes for doctors next year—e.g.

1. Doctors more than 6 feet.
2. Doctors less than 6 feet.
3. Working doctors.
4. Doctors with student at foot.

All entries to be properly qualified and on the Register.

Letters to the Editor

REAPPEARANCE OF TABOPARESIS?

SIR,—Some senior and experienced psychiatrists have recently had cause to give considerable thought to the topic of taboparesis. One British psychiatrist recently found that there was concern in responsible circles in America on the same topic. When the time-lag between primary infection with syphilis and the onset of taboparesis is considered, it appears possible that the recent virtual disappearance of taboparesis is due to the efficiency of arsenical treatment in the years before the large-scale employment of antibiotics.

It may be that cases treated in the early years of the antibiotic era have yet to develop taboparesis. The time factor suggests that the next few years may be particularly important in this respect. Recently, a senior psychiatrist with considerable experience of neurosyphilis had four cases referred to him within a very short period—more cases than he had seen for a very long time previously. Two of these cases could easily have been missed by a more junior man with little practical experience of taboparesis. Moreover, some of the old characteristic physical signs seem to be changing somewhat.

It may be hoped that fears of a reappearance of taboparesis on a considerable scale may prove groundless, but there appears to be reason for clinicians to be very alert on this topic, so that if an increase in the number of cases should occur, the sufferers from it may be diagnosed early and, therefore, successfully treated.

NOEL G. HARRIS
Chairman,
Public Relations Committee.

The Royal Medico-Psychological Association, London, W.1.

CHILDREN IN HOSPITAL

SIR,—In a lecture given to the Central Council for Health Education, Professor Illingworth (July 26) has made some extraordinary statements about infectious-diseases hospitals. Many of these provocative remarks were refuted at the conference but apparently with little effect on the subsequent publication of the lecture by the Council and by your journal.

Professor Illingworth's personal experience of infectious-diseases hospitals would seem, from his lecture, to be limited to the pre-war era. Only this can explain his recommendation that the great majority of cases of uncomplicated measles and scarlet fever should be nursed at home. Of course, this has been the common practice for many years and certainly these cases are only rarely admitted to the infectious-diseases units in the London area.

All would agree with his comment that children should not be admitted to infectious-diseases hospitals unless it is really necessary, a recommendation which would apply to children entering any hospital. It is difficult to see, however, what advantage would be gained in establishing isolation units at each general and children's hospital except in sparsely populated areas. The Royal College of Physicians' view, that in every pædiatric unit isolation accommodation is essential, is a wise one, considering the frequency with which such units go into quarantine with chickenpox and measles, but to convert existing general and children's hospitals, so that infectious cases can be admitted as routine policy, would merely duplicate facilities already in existence. The arrogant assumption that only a pædiatrician is capable of looking after cases of gastroenteritis is shown in its true light when one considers the large number of such cases which have been efficiently treated by the medical and nursing staff of infectious-diseases units over many years. Can it be that the pædiatric world, tiring of enuresis and metabolic rarities, is looking for fresh pastures?

The Professor's wildest assertion, "that a high proportion of children admitted to infectious-diseases hospitals are not suffering from an infectious disease at all", can only mean that he equates infectious disease with notifiable infectious disease, two entirely different matters. Admittedly some forms of pneumonia and meningitis are not infectious, but the majority, including many of the viral and bacterial varieties, are most certainly so. Can the infectivity of these conditions be determined at the time of admission? If it could, we would not be faced with the tragedy of paralytic poliomyelitis developing in a child admitted to a general children's ward for treatment of some other condition—an event not unknown in the experience of most physicians dealing with infectious diseases. Yet the polio virus has low infectivity in comparison with the Echo virus, to mention only one. No, Sir, cases of pneumonia and meningitis, in common with other infectious diseases, should continue to be admitted to isolation units for investigation and treatment, for only there can the interests of the individual and the safety of the community be reconciled.

R. T. D. EMOND
Physician-Superintendent.

Coppetts Wood Hospital, London, N.10.

SIR,—Professor Illingworth's lecture to the Central Council for Health Education contains some provocative assertions regarding infectious-disease hospitals. His statement that "the great majority of cases of uncomplicated measles and scarlet fever should be nursed at home" comes about twenty years out of date and belongs not only to a pre-antibiotic era but to a pre-war era. This has been the practice in Greater London, if not over most of the country, and has contributed to the great reduction in the number of available infectious-disease beds per thousand of the population over the past twenty years.

Professor Illingworth states "The aim of cubicles is the prevention of cross-infection, and we all know how regrettably they fail to achieve this." Cross-infection is most likely to occur in *Escherichia coli* infective gastroenteritis and salmonella infections in infants. Apart from these incidents cross-infection is no problem in infectious-disease hospitals where the cubicles are well planned and where the prevention of the spread of infection is instilled into all staff trained in these hospitals or units.

His inaccurate assertion that only a pædiatrician has experience of infectious diseases requiring specialised treatment (e.g., gastroenteritis) is quite out of place, bearing in mind the amount of good work that has been done throughout the years in infectious-disease hospitals. Gastroenteritis, which he quotes, and of which we saw so much in the past, has now ceased to be the problem it was in this country.

Could it be that, with the tremendous improvement in nutrition and in child health generally—partly contributed to by the public and school health services and education of parents, and partly by the advent of the antibiotic era—the pædiatric fraternity is looking for further spheres of activity, in which other people have worked when problems were greater than at present?

W. F. TWINING MCMATH.

Neasden Hospital, London, N.W.10.

IDIOPATHIC THROMBOCYTOPENIC PURPURA AND DISSEMINATED LUPUS ERYTHEMATOSUS

SIR,—We were interested to read an annotation on the treatment of idiopathic thrombocytopenic purpura (I.T.P.) in the *British Medical Journal* of July 20 which deals largely with two papers published by Dameshek and his colleagues.[1 2] These authors claim that approximately 25% of all patients with apparently typical I.T.P. in whom the spleen has been removed will eventually develop disseminated lupus erythematosus (D.L.E.). This is contrary to our own experience, which is given in our paper in *The Lancet* of Aug. 2. In none of the 42 cases of I.T.P. submitted to splenectomy, and followed up for periods of from 1 to 29 years, did the clinical features of D.L.E. develop. This is also our experience in a large series of splenectomies carried out on patients with portal hypertension and hæmolytic anæmia. We therefore consulted the two papers by Dameshek and his colleagues, and we find that, although the figure of 25% is given by these authors, they supply no details of the cases and no supporting evidence that splenectomy either caused D.L.E. or hastened its onset.

In the second paper an account of only 1 patient with "idiopathic" thrombocytopenic purpura is given. A study of this case-record makes it clear that the patient had stiffness, limited movement, and spindling of the finger joints, and fever, coincidental with the onset of the thrombocytopenic purpura. Accordingly it seems to us likely that a collagen disease was already in being. This is admitted by the authors who state that ". . . the possibility of a more fundamental disease such as D.L.E. was considered". Whether the severe manifestations of D.L.E. which developed 4 months after splenectomy were the result of the operation or were due to a spontaneous progression of the disease, can only be a matter of conjecture.

Lastly, we agree with Dameshek and his colleagues that steroid therapy should be the first line of treatment both in acute and chronic I.T.P. We do not agree, however, that splenectomy is potentially dangerous or of little therapeutic value, since none of our cases developed D.L.E., while 75% of our "short history" cases of I.T.P. and 50% of our "long history" cases have remained well for periods which in some cases extend over 12 years.

STANLEY DAVIDSON
A. I. S. MACPHERSON.

Edinburgh.

ASPIRIN AND PEPTIC ULCER

SIR,—The possibility that aspirin may cause hæmorrhage is a matter of considerable importance to patients who have a chronic peptic ulcer, or the diathesis for acute gastric ulceration. It is therefore unfortunate that Dr. Allibone and Dr. Flint (July 26) should "conclude that aspirin, although a gastric irritant, is a rare cause of hæmatemesis" when their data do not warrant such a conclusion. Aspirin has been used so extensively and for so long that it cannot come as a surprise that 59 of their 129 controls took the drug, within two weeks of admission to hospital, without ill effect. On the other hand, who can say how many of the 61 "series" patients who had taken aspirin precipitated their hæmorrhage (or perforation) by so doing? It is presumably among the ulcer group alone that the risk exists, and therefore a controlled investigation of this problem should be confined to such patients.

Department of Social Medicine,
Trinity College, Dublin. ROY M. ACHESON.

ULCERATIVE COLITIS

SIR,—In psychosomatic disorders there is to date a woeful lack of adequate research, and accordingly even the most tentative hypotheses have too readily gained the status of inviolable laws. Dr. Sim and Mr. Brooke (July 19) are, therefore, to be congratulated on their attempt to test current psychosomatic hypotheses with respect to ulcerative colitis.

Some methodological questions, however, arise. For instance, do the members of the Ileostomy Association represent a fair cross-section of the ulcerative-colitis population? Further, the questionnaire method—as compared, for example, with the standard interview—may involve significant limitations. The reader would have been further enlightened if the items of the questionnaire had been described in detail.

Above all, a retrospective survey of the order of appearance of the symptoms of ulcerative colitis (which often arose many years previously) is, as the authors themselves concede, open to error. Not only is heavy reliance thus placed upon the patients' memories but a distortion factor may be introduced if conflict-producing situations and emotional disturbance become subject after many years to repression and dissociation. That this is liable to happen is indicated by Bastiaans and Groen,[1] who comment thus upon their study of psychological factors in ulcerative colitis patients: "Usually the occurrence of such an event [i.e., an acute emotional trauma within 48 hours before the illness began] was denied when the patients were asked outright, during the first interview, if anything had upset them. When, however, they were given an opportunity to give their life history and encouraged to talk freely about their present situation they told of such events."

Dr. Sim and Mr. Brooke may have cast grave doubt upon certain hypotheses regarding ulcerative colitis, but this should not be mistaken for the death-knell of a psychosomatic approach to this disease. Only long-term longitudinal studies of a prospective nature as well as careful experimental investigations, rather than cross-sectional studies, will permit a sober appraisal of possible emotional factors in this puzzling disease.

Southern General Hospital,
Glasgow. A. BALFOUR SCLARE.

SIR,—Dr. Sim and Mr. Brooke (July 19) make a big sweep with a small broom when they conclude that the absence of diarrhœa as an initial symptom of ulcerative colitis leaves "little evidence . . . to support existing psychosomatic hypotheses of the origin of the disease." For only in very specious and theoretical misapplication of Freudian theory can anyone so far turn their backs upon the disease in search of its causation.

Respectable psychosomatic theories of ulcerative colitis must be based upon the known responses of the colon to emotion or the association of abnormal emotional constitution with the disease.

The disturbances of colonic function most clearly induced by emotion have been (*a*) vascular and secretory changes in the mucosa, first described in dogs,[2] but repeatedly observed in man [3 4]; and (*b*) changes in the tone and contractility of the colonic musculature. Colonic spasm has been shown to be capable of producing rapid ulceration of the colonic mucosa in dogs.[5]

The more durable of existing psychosomatic hypotheses are

1. Dameshek, W., Reeves, W. H. *Amer. J. med.* 1956. **21**, 560.
2. Dameshek, W. et al. *J. Amer. med. Ass.* 1958. **166**, 1805.

1. Bastiaans, J., Groen, J. *in* Modern Trends in Psychosomatic Medicine; p. 111. London, 1959.
2. Drury, A. N., Florey, H., Florey, M. E. *J. Physiol.* 1929, **68**, 173.
3. Almy, T. P., Kern, F., Tulin, M. *Gastroenterology* 1949, **12**, 425.
4. Grace, W. J., Wolf, S., Wolff, H. G. *J. Amer. med. Ass.* 1950, **142**, 1044; *Gastroenterology*, 1950, **14**, 93.
5. Lium, R., Porter, I. E., *Arch. intern. Med.* 1939, **63**, 201.

based upon well-observed facts. In addition to emotionally induced changes in mucosa and muscle these include the many studies in emotional and personality types found in ulcerative colitis, from the pioneer clinical observations of Hurst [6] through the character studies of the thirties to the, in some cases, more detailed work of the past decade or so. A few other studies not mentioned by Dr. Sim and Mr. Brooke are listed below.[7–9]

The presence or absence of diarrhœa as an initial symptom does nothing whatever to detract from these many deep and massive studies of the psychogenesis of ulcerative colitis. To all who have studied it carefully from both aspects this disease is so strikingly based upon a complex of body-mind relationship that it is distressing to find two modern writers who are willing to think such a frail criterion as the time of arrival of liquid stools can leave us " little evidence " of the deeply distorted characters and the profound physical and mental susceptibilities and sensitivities that are causally connected with the symptoms in sufferers from this disease.

Dorrington Grove,
near Shrewsbury. RANYARD WEST.

"EXPERIENCE AND INCENTIVE" AWARDS?

SIR,—The principle of differential payments to general practitioners for the *quality* as distinct from the *quantity* of their work appears at last to be receiving serious attention. The stumbling-block of " merit " awards lies in the difficulty of finding a method to assess merit. I do not believe that any system which depended primarily on the assessment of the merit of one practitioner by another practitioner could possibly succeed. The idea that a board of consultants might do it would surely be as embarrassing to the consultants as it would be to the general practitioner.

May I suggest therefore that the word " merit " be dropped altogether and that an alternative " experience and incentive " award be considered?

The difference in such an award is that it would not be beyond the reach of all G.P.s at some time in their careers. For this reason I believe it would be more generally acceptable. If payment for it was met out of some fund other than the central pool it could play a big part in what should be its *main* purpose—i.e., the promotion of good general practice.

For such an award only criteria that are fairly easily assessed could be used. I would suggest:

(1) 10 years' experience as a principal.
(2) A high standard of surgery premises and equipment.
(3) A list of patients not below a certain minimum, nor yet above a certain maximum considered locally suitable.

To those critics of such yardsticks (e.g., Burdon [10]) I would point out that while experience is no guarantee of merit, it is fair to assume that every doctor is a better doctor for 10 years' experience (indeed general practice is about the only branch of medicine in which experience is not rewarded).

Again, whatever his capacity, any doctor can surely give a better service to 2500 patients than he can to 3500. Moreover, an incentive to reduce his list would encourage him to take in a partner, or form a group practice. Similarly, good premises and equipment, though no guarantee of good work, are essential tools for the job.

A fourth element, to form the incentive side to such an award, is more difficult to define. I suggest that it should amount to an expression of willingness on the part of the individual to maintain his efficiency. This would take different forms. Some like to take refresher courses. Others prefer to engage in research or to be clinical assistants at nearby hospitals—or to engage in some other form of postgraduate training. The essential thing I suggest is that, to qualify for such an award, the doctor would have to bring evidence of his efforts to improve his efficiency in one way or another. I see no harm in the idea that such evidence should be produced again, say, every seven years—so that the grass shall not grow, &c.

Stratford-on-Avon. E. O. EVANS.

6. Hurst, A. F. *Guys Hosp. Rep.* 1921, **71**, 26.
7. Moscheowitz, E. *Amer. J. med. Sci.* 1943, **206**, 576.
8. Murray, C. D. *ibid.* 1930, **180**, 239.
9. West, R. *Lancet* 1946, ii, 899.
10. Burdon, J. F. *Brit. med. J.* 1958, ii, Suppl. p. 27.

CARDS FOR PATIENTS TAKING STEROIDS

SIR,—It is recognised that sudden withdrawal of steroids in patients undergoing long-term treatment may be dangerous, particularly when such patients have been subjected to sudden stress, such as an acute illness, accident, or emergency operation. In these circumstances it may be of vital importance for the physician or surgeon responsible for the patient's immediate care to be made aware that the patient has been on steroid therapy, the form in which it is being administered, and the daily dose.

The education subcommittee of the Empire Rheumatism Council gave this matter consideration at a recent meeting and reached the conclusion that a useful purpose would be served by the issue of a card to patients receiving steroids, stating the preparation in use and its daily dose. The hospital or clinic supervising the patient's treatment and the name and telephone number of the family doctor should also be recorded along with simple instructions to the patient.

I have been instructed by my committee to bring this matter to your notice, as the Empire Rheumatism Council would be prepared to make a supply of these cards available to any physician who might wish to use them.

Faraday House,
8-10 Charing Cross Road,
London, W.C.2.

J. J. R. DUTHIE
Chairman,
Education Sub-committee,
Empire Rheumatism Council.

VENTRICULAR SEPTAL DEFECT

SIR,—Your leading article of July 12 favours a classification based primarily on catheter studies and necropsy. Open heart surgery enables one to obtain a more physiological appreciation of the anatomical defects; 36 ventricular septal defects have been repaired in the past year at this hospital and as a result it is suggested that the presence or absence of an infundibular pulmonary stenosis plays a major part in the pathological physiology of ventricular septal defects, and that therefore this factor should be included in such a classification.

Full cardiac catheterisation figures and operative details are available on 22 of these 36 cases. They suggest that the following classification be used:

(1) The pulmonary-artery pressure, right ventricular pressure, and systemic pressure are of a similar level. These cases have no obstruction to a shunt of blood from the left ventricle to the right ventricle, and they have no obstruction to the outflow tract of the right ventricle.

The cardiac catheter passes with ease into the pulmonary artery. At surgical repair, though there may be some work hypertrophy of the infundibular muscle, the outflow tract is adequate and no resection of muscle is required.

We have had 12 such cases, with 4 deaths.

(2) The pulmonary-artery pressure is low; the right ventricular pressure high, approximating to the left ventricular pressure. No cyanosis is present.

These cases are frequently referred to as an " acyanotic tetralogy of Fallot ". The cardiac catheter may pass with some difficulty into the infundibular chamber and at surgery the physiological barrier of muscle which protects the lungs from the raised ventricular pressure may be seen. Resection

of this infundibular stenosis is a requisite part of the operation, coupled with repair of the ventricular defect.

6 cases with 3 operative deaths.

(3) The pulmonary-artery pressure is low and the right ventricular pressure is low. The systemic pressure is normal.

These are the small muscular defects of the maladie-de-Roger type. We have had 4 cases, no deaths.

The inclusion of the second group of cases, the "acyanotic tetralogy of Fallot", under the heading of ventricular septal defect is warranted by the fact that group I and group II merge into one another. They are both amenable to surgical treatment. This differentiates them from the advanced cases of Fallot's tetralogy where the pulmonary artery is of small size and which, even after repair of a ventricular defect and removal of any right outflow-tract obstruction, may well be unable to take the increased flow of blood.

Department of Surgery,
Stanford University School of Medicine. A. G. NORMAN.

NO MORE NEOLOGISMS?

SIR,—We are grateful to you for your defence of necessary neologisms. Indeed, we find Sir George Pickering's criticisms (July 26) of the use of "hæmorheology" a little difficult to follow.

It is, of course, true that many great men have studied the flow of blood and the mechanical properties of blood-vessels before a special term for this field of work was needed. But surely many doctors must have tried to find causes and cures for diarrhœa and amenorrhœa long before the Greek root "rheo" was so happily introduced to describe these conditions. Moreover, Sir George, although quoting our definition for hæmorheology, appears to restrict this term to "the blood-flow in relation to the vessel wall", thus overlooking the fact that much more than this is implied.

Rheology, the science of the deformation and flow of matter, forms a part of the official title of scientific societies in many countries. The Third International Congress on Rheology will be held in Germany in two months' time. The name of this branch of physics is almost identical in all four of the official languages of that congress—English, French, German, and Russian—and, of course, in many other languages. Few people can fail to know the meaning of the root "hæmo". The combination of these two Greek roots seems to be indicated if we are to be saved the nuisance of continually repeating the full definition of this branch of science.

We, as hæmatologist and rheologist respectively, therefore, move that the term "hæmorheology" be accepted as a very necessary neologism.

Medical Research Laboratories,
Charing Cross Hospital,
London, W.C.2. A. L. COPLEY.

National Institute for Research
in Dairying,
University of Reading. G. W. SCOTT BLAIR.

SIR,—Sir George Pickering and Dr. Pappworth (July 26) raise the question of an ever-expanding, often grammatically objectionable, medical terminology. I would emphasise that these two aspects—the tendency of new terms to increase with time, and the suitability of the new word—must be kept distinct in our minds, especially when we reach the point of protest.

The first reflects, surely, an inherent characteristic of (scientific) development in general. Discoveries in all fields of medicine bring with them new names and we *have* to welcome them! But also, and this is of at least equal importance, the reappraisal of a difficult problem may be a perfectly good reason for a new word, which, when coined, helps to focus and integrate the new notion.

Just as the new terms come into use the old ones go into disuse and the survival of a new term depends entirely on the mood, tastes, and existing needs of the people for whom it was intended. Beneath this normal mechanism of word production, however, there seem to act, especially during the last few decades, gross exaggerative undercurrents due, I suspect, to three main reasons:

(*a*) Specialisation tends to take the form of a closed cult and all new members have to go through a period of initiation in which the apocryphal words of the cult must be mastered; clearly, such words have a high magical value (for they signify the concentrated wisdom of the "specialty"), become irresistible in their perpetual use, dominate the predisposed members of the cult, and, in moments of mystical ecstasy, may lead to new products—Greco-Latin hybrids, or even full-blown neologisms should the right mutation take place.

(*b*) Words which are quite unknown, or at least difficult to understand with certainty, foreign phrases and proverbs, Latin-Greek-French-German-or-Oriental-medical-terms, and their hyphenated permutations, have such an appeal that their use in a medical paper appears to strengthen its importance, repel criticism and, perhaps, make its publication a little more probable. In this respect also, some writers seem to aspire to associate their names with the introduction of a linguistic novelty; thence the abundance of terms like cephalalgia rather than headache.

(*c*) A neologism perpetrated in Greek, Latin, Greco-Latin, &c., is permissible if not advisable; a neologism in one's own language—a strangely difficult thing—is usually considered as an ominous sign of a very serious mental disease.

I have not drawn any semantic boundaries around the words jargon, neologism, neology, term, nomenclature, or even barbarism. I expect Professor Pickering might enlarge upon this in his promised communication on the matter; such a semantic tidying up will put things in their right perspective and, I hope, might substantiate my foregoing views about the natural production of scientific words and the unnatural exaggeration of the present day towards jargon (i.e., towards terms known only to members of a certain group).

Another point that may well emerge from such a study is that when medicine stopped being written in Latin, a conscious effort was made by the doctors of many countries to introduce in their scientific languages terms of Greek or Latin origin with the view to continuing a sense of international understanding in the writings of medical men. Such terms (e.g., catagma) still appear in medical dictionaries but are completely out of use and should not be confused with the tendency to create jargons—a much more complex phenomenon.

Turning to the "suitability" of the new word, it is here that the most striking monstrosities are perpetrated against clarity, elementary etymology, and euphony. The first two are, of course, more important and mistakes in them are invariably due to ignorance of the materials employed. To take the example Professor Pickering wants (so very understandably) to challenge, Dr. Copley having studied the properties of blood-flow and factors affecting it, felt the need for a comprehensive and precise term for this subject; thus, "hæmorheology" was coined, clearly of Greek material. The word the Greeks have for "the flow", however, is not—*rheo* (ῥέω = I flow) but ῥοή, which should of necessity be transliterated as "rhoe". This probably appears much like roe and perhaps unsavoury for the occasion.

I want to emphasise that this type of offence of being obscure and linguistically inaccurate is almost lost in the wave of the

much more serious offence of substantial error: natriuresis, (which Professor Pickering quotes) simply means "excretion of sodium" and not "increased excretion of sodium" which the author wanted to say. "Kaluresis" is doubly wrong for, at least, it should read "kaliuresis" if not "hyperkaliuresis" which is the accurate, although not welcome, term.

From Dr. Pappworth's interesting anthology, about 52% of the first list are legitimate, though perhaps not generally used terms; the words neurosophical, dysraphicus, undervascularised, transfusionist, and thoracologist are just clumsy and/or obscure while allergology and ataralgesia are linguistically wrong (they "mean" allergiology and ataraxalgesia).

I do not think I can agree with Dr. Pappworth's views on the suffix -itis. "Inflammation" is quite accurately translated from Greek in which *φλέγμα* means flame, heat; in inflammation, therefore, redness and swelling usually follow. (Hence *φλεγμαίνειν* also means "to fester"). The looseness of the suffix -osis or -pathy is, I feel, well in line with our increasing knowledge of the conditions to which they are attached.

Few would disagree with your view that Natural Selection is a decisive factor in the fate of neologisms. But how about jargon? There is much more there than the venturing of an epithet or the display of simple affectation. Not only it reflects psychological reactions (some of which I half-humorously mentioned before) but it possesses some of the dubious virtue of scientific "shorthand," at a moment when science is getting more and more longhanded. Professor Pickering and all academic teachers can fight jargon mostly by their own example, expressing their views simply and understandably, so that clarity replace undesirable jargon in all medical branches.

The Maudsley Hospital, London, S.E.5. G. M. JACOBIDES.

SIR,—As an addendum to my letter of July 26 I should like to include the following words, taken from *The Lancet* during 1958:

Typology	natriuresis	immunoconglutinin
nomothetic	chloruretic	reticulohistiocytosis
electroplexy	hepatocerebral	proteinosis
renoprival		

Immunoconglutinin and reticulohistiocytosis represent two of the ugliest polysyllabic artificial neologisms ever perpetrated.

Natriuresis and chloruretic are two of the words singled out by Sir George Pickering (July 26), and renoprival suggests that renal specialists are amongst the worst offenders. A *Lancet* article of 1957 contained the word nephritogenic, which apparently has nothing to do with the creation of kidneys but describes those organisms which cause renal lesions; and *The Lancet* (1952) used the term *tubulorrhexis*.

Hiding behind the cloak of somebody else's authorship by putting quotation marks around a word is rarely justifiable, because it often merely perpetuates the use of a bad term. Examples of this were the use of the word proteinaceous in that article which discussed proteinosis, and a *Lancet* article of 1953 which contained the word metabolician and another of 1955 mentioned dolichostenomelia and phenocopy, all in quotation marks.

In 1954 an author repeatedly used sideropenic where most of us would have used the accepted phrase, iron deficiency. And in a more recent article[1] the word clubbing, which was used in the title, was later replaced by acropachy. Several questions occur to me:

(1) What is the difference between acropachy and pachyairia, another term which I have come across in my reading?

(2) Is acropachy synonymous with clubbing, and, if not, what are the other causes of it?

(3) Does acropachy describe only part of the clubbing phenomenon? If so, what is the purpose in giving the components of clubbing different names?

1. Freeman, A. G., *Lancet*, July 12, 1958, p. 57.

Another problem which confronts the medical reader is the replacement of well-accepted and known names by new terms which the author thinks more accurate. For example the replacement of the term fibrocystic disease of the pancreas by either mucoviscidosis or mucoid dysporia. Some authors, wishing to point out the well-known facts that periarteritis nodosa (first named by Kussmaul and Meir as long ago as 1866) is probably neither inflammatory nor necessarily associated with nodules, have coined the following titles for this disease: polyvasculitis; allergic granulomatous angiitis; polyarteritis nodosa; necrotising arteriolitis; hypersensitivity angiitis.

Most authors would agree that there are clinical gradations between typical angina of effort and coronary thrombosis. Does this justify a new term? I would say, "No". If it does, what should it be? I have come across the following answers: status angiosus; severe angina; angina decubitus; infarction without infarction; prodromal coronary artery occlusion; coronary failure; acute coronary insufficiency; intermediate coronary syndrome. Perhaps I am wrong in considering all these are one and the same thing.

London, W.1. M. H. PAPPWORTH.

SIR,—There is plenty of room for new words in medicine, and we are all indebted to you for your defence of literary freedom. The danger of your journal setting out to "uphold the dignity and purity of the English language" by censorship is illustrated by Dr. Pappworth's letter of July 26, nearly all of which can be disputed.

It is proper that new concepts and classifications should be borne by new words, untarnished by confusion and misuse. What is the alternative? Will it please your correspondents if we give new meanings to old words, and will they prefer the confusion if advances in knowledge slip, half digested, into our minds, disguised in familiar forms. We are fortunate in medicine that a technical term is unmistakable, and does not, as often in subjects like philosophy and economics, masquerade as an everyday word or phrase. Thus, the reader is made aware of his ignorance, and consequent loose thinking is discouraged.

Musicians have complained about their lack of technical terms, and its cramping effect. A growing subject needs a fluid language, with words passing freely in and out of common use. For example, when "hyperchromic anæmias" were redescribed as "macrocytic anæmias" a rational understanding of these diseases became easier.

Perhaps one day we may have an *Oxford Medical Dictionary* on historical principles, showing which words are archaic or obsolete, as well as those that are superfluous, misleading, or so ambiguous as to be unusable in precise writing.

The real problem is to avoid new words that are unnecessary or ugly. If censorship is unacceptable, there is need for a forum where they can be examined, so that Natural Selection can work quickly. Such publicity should discourage light-hearted word-making, and also advertise the useful new words, with their associated advances in knowledge. It would also in time clarify the indications for new words. Perhaps *The Lancet* could find space for an occasional discussion on these lines.

For the ugly or ill-chosen words, prevention is easier than reform (although the history of "valvulotomy" shows that reform is possible). The available reference works (Dorland's *Medical Dictionary*, Ffrangcon Roberts' *Medical Terms*, and Jaeger's *Source Book of Biological Names and Terms*) are not widely known, and their users may produce some very clumsy words indeed. Euphony is as important as a meticulous classical derivation, and perhaps we should study the practice of drug firms in naming their products, rather than dictionaries of classics and etymology.

There is need for another Gowers to write on *Plain Medical Words*, and show us how to make new ones short and lucid.

Glasgow. C. MACKENZIE GRANT.

THE PREDICAMENT OF THE BLADDER

SIR,—We have thoroughly enjoyed Mr. Downie's letter of June 21. His warm sympathy for this "unfortunate organ" is entirely understandable. As a matter of fact, of course, the various fates to which the bladder is subject represent merely a portion of the ills to which the genitourinary system as a whole is heir. Mr. Downie might be interested in a statement made some time ago by a philosophic friend of ours, who remarked that the poor design and mechanical construction of the system may be used as an argument in favour of polytheism. When asked why, he explained, "It was obviously designed by a *committee* of gods."

D. L. OPDYKE
F. H. SNYDER
J. G. VOSS.

Cincinatti, Ohio.

Obituary

ALFRED ARTHUR EDWARD NEWTH

O.B.E., M.B. Lond., D.P.H.

Dr. Newth, formerly principal school medical officer for Nottingham, died on July 30 at the age of 70.

He was the son of a general practitioner who practised in Haywards Heath, and he was educated at Epsom College and Westminster Hospital. After qualifying in 1911 he held house-appointments at the Westminster Hospital, and at hospitals in Wolverhampton and Derby, and in 1914 he was appointed school medical officer to the Nottingham education authority. Soon afterwards he joined the R.A.M.C., serving in France, and he did not return to Nottingham till 1918. He remained with the city's school medical service, becoming in due course principal school medical officer, until he retired in 1954. He was appointed O.B.E. in 1952.

The care of handicapped children was always his special concern, and in his retirement he showed his practical interest in mental health by becoming a medical officer at the Mapperley Hospital, Nottingham. He was a member of the medical advisory committee of the British Council for the Welfare of Spastics. He also continued to serve as a valued member of the Ministry of Education's advisory committee. Of his long and cordial relationship with the Ministry J. E. U. writes:

"Newth's sound judgment and his exceptional insight into the problems and needs of the handicapped child brought us into frequent consultation and I shall always remember the invaluable help he gave as a witness to the Committee on Maladjusted Children. As principal medical officer of Nottingham, he stood at the head of one of the foremost school health services in this country, a service which had been developed by his enterprise and efficiency. But his interests covered a much wider field than that of his own county borough. He was indefatigable in attending meetings, conferences, and refresher courses, and he did much to inspire his colleagues with his own enthusiasm for the welfare of school-children."

Dr. Newth was an able speaker and writer, and the School Health Service Group of the Society of Medical Officers of Health owed much to him as secretary and president. Of this work H. M. C. writes:

"Dr. Newth was untiring in his endeavours, and his preparation of the papers for the meetings was an indication of his energy and acumen. He had an excellent and well-stored brain, and though he was meticulous in details, the memoranda which he prepared for guidance had a lively style. So much did his colleagues appreciate his service for the group that a dinner was held in his honour, when a presentation was made to which colleagues from all over the country had contributed.

"His interests were not confined to school health; he played an excellent game of golf and one recalls with pleasure his expert comments on visits to Twickenham. He was also a skilled craftsman. Despite his knowledge and erudition he was by no means the dull administrator, and his friends will remember his unfailing good humour, tact, and pleasant chuckle."

Mrs. Newth is also a member of the medical profession.

MALCOLM ARTHUR SMITH

M.R.C.S.

Dr. Smith, who was an authority on the reptiles and amphibia of Eastern Asia and of the British Isles, died at his home at Ascot on July 24 at the age of 82.

He qualified from Charing Cross Hospital in 1898 and shortly afterwards went to Siam. For the next twenty-five years he practised in Bangkok where he was medical officer to the British Legation. After being attached unofficially to the Court of Siam for some years he was appointed the official court physician. In this capacity he saw the celebrated Queen Mother, Queen Saowapa, almost daily. He described this part of his life in his book *A Physician at the Court of Siam* (1946).

Throughout his life he was interested in zoology, and particularly in herpetology, and made many field expeditions in the Far East in pursuit of his hobby. Over 100 papers on the reptiles and amphibia of the East and later of Great Britain (his book on British reptiles and amphibia is the standard work on the subject) testified to the scope of his knowledge and work. Most of his collection of 9000 preserved specimens of amphibians and reptiles he presented to the British Museum of Natural History, where he worked for some thirty years after his return to this country. He was for nearly twenty years secretary of the zoological section of the Linnean Society and also the first president of the British Herpetological Society, which was founded in 1947.

He married Miss Eryl Glynne in 1921 and had three sons, the eldest of whom is a doctor. Two of his sons and his second wife survive him.

Sir ARNOLD STOTT

R. W. B., who was one of Sir Arnold Stott's last house-physicians at Westminster, sent these reminiscences to show "his real stature as a teacher":

The ward round reached the bed of a patient with spasmodic bronchial asthma and Sir Arnold, having heard the history, asked successively the student, house-physician, registrars, and ward sister "What is in his pillow?" Nobody knew. The next move was dramatic and unforgettable. "Sister, your scissors." The pillow was slit open and feathers shaken over the ward round. "Feathers" was the only comment—but no-one present could ever forget the ubiquitous role of foreign proteins in allergic disorders. On another occasion diarrhœa had been present for some days in a patient having medical treatment for a peptic ulcer. The student's history was heard with a slightly impatient air, his examination provoking the response "And what was revealed by digital examination of the rectum?" Silence followed broken by Sir Arnold, "Sister, a glove." Rectal examination was accompanied by the question "What is a scybalum?" A further silence, then, incredulously, "You *don't* know?" A still further silence was broken by a rattling sound as a scybalum was rolled along the wooden floor. Crude? Unnecessary? Aggressive?—but then so is disease, and the comfort brought to patients later by those present through awareness of the possible agonies of constipation could be said to justify it.

Accurate and economic use of words was another lesson Sir Arnold repeated time and time again. "What diet is he having, Dr. ——?"

"A light diet, Sir." Pause, then "Phosphorescent?" Or the cutting interruption when told the fauces are injected: "Who injected them?" or when told a patient had a temperature: "Everyone has a temperature. Do you mean pyrexia?" These remarks were delivered quietly and almost resignedly and never caused personal offence. "You have told me the joint is swollen," he said to one student. "Now tell me the degree. Is it slight, moderate, or considerable?"

On one occasion Sir Arnold wrote a prescription putting the wrong date, which was pointed out by sister. He turned to the student at his elbow accusingly. "You saw me put the wrong date and let me do it." The student replied: "Since *you* wrote it how could *I* think it wrong?" Then there was a pause and then: "That was a good remark, the first for some time. How long have you been on my firm?" At that time a clinical firm consisted of six students and he frowned if anyone tried to tag on. "Six is enough for one patient," he once said, "and I haven't enough knowledge for more."

The sad day came when the house job was over. It was at the end of tea in Sister's office. "I consider you have been a good house-physician," he said, which from him was praise indeed. "Slight, moderate, or considerable?" I ventured to inquire. "You know the answer to that better than I—but thank you for all your hard work." He smiled, shook hands, and walked away.

Lord WEBB-JOHNSON

F. R. P., who studied medicine at Owens College, Manchester, and at the Middlesex Hospital, writes from Bombay:

Lord Webb-Johnson, when he was just Mr. Arthur Webb-Johnson, an easy-going jovial young man, was my tutor and guide in surgery. Since then, these forty long years and more, we have in a way grown up together, for up to the end of his life we corresponded with each other as colleagues and friends. Enough has been said about his good qualities, his professional abilities and public work; but as an Indian, deeply grateful to him for his many kindnesses to a lonely foreign student in his country, I add one more tribute to this great Englishman to whom, along with others such as Sir Victor Bonney, Sir John Bland-Sutton, Sir William Sinclair, and Sir William Fletcher Shaw, I owe all I have achieved in my profession.

Appointments

BEGG, ROSEMARY A., M.B. Edin., D.P.H.: administrative assistant county M.O., Kent.

BREWERTON, D. A., M.D., B.Sc. McGill, M.R.C.P., D.Phys.Med.: consultant physician in physical medicine, Westminster Hospital teaching group, London.

COLES, H. M. T., M.D. Lond., M.R.C.P., D.C.H.: consultant pædiatrician, Westminster Hospital teaching group, London.

COOPER, C. F., M.D. Lond., M.R.C.P.: part-time consultant physician, Wembley Hospital.

HOLLOWAY, J. J., M.B., N.U.I., D.P.H.: deputy M.O.H. and deputy principal school M.O., Northampton.

LLOYD, V. A., M.B. Birm., D.P.H.: assistant M.O.H., Sutton Coldfield area, Warwickshire.

THOMPSON, ELEANOR A., M.R.C.S.: assistant M.O.H., north-western area, Warwickshire.

Leeds Regional Hospital Board:

BENIANS, R. G., M.D. Cantab., M.R.C.P.: assistant geriatrician (S.H.M.O.), Bradford A and B hospital groups.

BIRD, J. D., M.B. Sheff., F.F.A.R.C.S., D.A.: part-time consultant in anæsthetics, Hull and East Riding hospital groups.

BURBURY, WINIFRED M., M.B. Lond., D.P.M.: consultant in child psychiatry, Wakefield and Dewsbury education committees.

EASTWOOD, John, M.B. Lond.: assistant pathologist (S.H.M.O.), Huddersfield hospital group.

LEESE, STEPHANIE M., M.B., B.Sc. Lond., D.P.M.: part-time consultant in child psychiatry, Wakefield and Dewsbury education committees.

LITTLE, J. C., M.B. Brist., M.R.C.P.E., D.P.M.: consultant in psychiatry, Leeds A and B hospital groups.

MATHESON, T. S., M.B. Edin., F.R.C.S.E.: consultant in general surgery, Otley hospital group.

MOYES, A. H., M.B. St.And., D.P.M.: assistant psychiatrist, Clifton Hospital, York.

POLLOCK, A. V., M.B., B.Sc. Cape Town, F.R.C.S.: consultant in general surgery, Scarborough, Bridlington, Malton, and Whitby hospital group.

QUINLAN, A. G., M.B. Lond., F.R.C.S.: part-time consultant in orthopædic surgery, Scarborough, Bridlington, Malton, and Whitby hospital group.

SACKER, L. S., M.B. Lond.: consultant in pathology, Hull A and B hospital groups.

WILSON, PETER, F.R.C.S.E., D.O.M.S.: consultant in ophthalmology, Huddersfield hospital group.

Notes and News

DISTRICT MENTAL HEALTH SERVICES

EARLIER this year Dr. Joshua Carse described in our columns[1] the first ten months' work of the experimental outpatient and domiciliary service which is being offered to mental patients in Worthing. The service is based on Graylingwell Hospital, Chichester. In a fourth interim report on the scheme he compares the results for the first six months of 1958 with those for the first six months of 1957 (which were also the first six months of the service). The total number of patients has fallen from 721 in 1957 to 657 in 1958 and the number of new patients from 699 to 618. But this reduction is largely among the younger people and the number of patients over sixty-five fell by only 10. Though the care of this group remains one of the problems of the service, Dr. Carse is able to report that of the 181 elderly patients referred to the service only 46 were sent into hospital.

The success of the service at Worthing, which is 22 miles away, encouraged Graylingwell Hospital to start another district service in Chichester itself at the beginning of this year, and in the first six months 510 patients used the service of whom only 124 were admitted to hospital. Together the services at Worthing and Chichester cover three-quarters of Graylingwell Hospital's catchment area, and in the first six months of their joint existence the number of admissions to the hospital was 382 compared with 678 in the first six months of 1956 before the start of the scheme. Both at Worthing and at Chichester the services rely heavily on the support of the family doctors who have taken a great interest in the experiment. At their request a course of weekly seminars was started in Worthing last May on psychotherapy and the general care of the neurotic patient.

University of Cambridge

On June 25 the degree of B.CHIR. was conferred on G. C. Sutton.

University of London

Dr. W. J. H. Butterfield has been appointed to the chair of experimental medicine at Guy's Hospital Medical School.

Dr. Butterfield, who is 38 years of age, studied medicine at Oxford University and at Johns Hopkins. He graduated B.M. in 1945 and took the M.R.C.P. two years later. After holding a junior lectureship in pathology in the University of Bristol, he took up a house-appointment in the Medical Research Council burns unit at the Birmingham Accident Hospital. In 1949 he joined the scientific staff of the Medical Research Council. He visited the United States in 1950–51 and held a research fellowship at the Medical College of Virginia, to investigate metabolic effects of thermal injury. Since his return to this country he has worked at the M.R.C. clinical research unit at Guy's Hospital. His published work includes papers on flashburns and the action of the sulphonylureas in diabetes. He was associated with the biological investigations at atomic tests in Australia in 1952 and 1956 and was appointed O.B.E. in 1953.

University of Manchester

The Wellcome Trust has given the university a mobile radiographic and laboratory unit which is to be used by the departments of rheumatology and occupational diseases for field investigations.

Society for the Study of Addiction

At a council meeting of this society, the following honorary officers were elected:

President: Prof. A. D. Macdonald; *treasurer and secretary:* Dr. Ellis Stungo; *organiser of meetings:* Dr. W. R. Bett.

Rockefeller Grants

Recent awards by the Rockefeller Foundation include a grant of $35,000 to a research group at London University studying heredity and genetics in mammals, and a grant of £12,000 to Dr. Dorothy Hodgkin of Oxford University for her investigation into the structure of insulin.

1. Carse, J., Panton, N. E., Watt, A. *Lancet*, 1958, i, 39.

Royal College of Physicians of London

At a comitia of the college on July 31, with Dr. Robert Platt, the president, in the chair, Dr. Saul Adler was admitted to the fellowship of the college (in absentia). The Murchison scholarship for 1958 has been awarded to Dr. L. G. Whitby. The following were elected officers for the coming year:

Censors: J. R. H. Towers, E. R. Boland, E. R. Cullinan, J. C. Hawksley. *Treasurer:* R. R. Bomford. *Registrar:* Sir Harold Boldero. *Harveian Librarian:* Sir Charles Dodds. *Assistant Registrar:* J. R. Ellis. *Library Committee:* C. E. Newman, William Brockbank, W. S. C. Copeman, W. H. McMenemey. *Finance Committee:* L. C. Martin, J. F. Stokes, J. W. D. Bull.

The following were elected to the panel of examiners for the membership examination:

Terence East, Donald Hunter, Sir Russell Brain, J. Forest Smith, L. B. Cole, J. L. Livingstone, A. C. Hampson, Lord Cohen of Birkenhead, A. M. Cooke, T. C. Hunt, H. K. Goadby, F. P. Lee Lander, W. D. W. Brooks, S. J. Hartfall, J. G. Scadding, M. L. Rosenheim, Horace Joules, Kenneth Robson, Arthur Willcox, Alan Kekwick, Una C. Ledingham, J. F. Stokes, William Phillips, W. Melville Arnott.

The following lecturers were appointed:

Sir Russell Brain (Harveian orator), Alan Kekwick (Bradshaw lecturer), E. J. Wayne (Lumleian), W. S. Peart (Goulstonian), P. L. Mollison (Oliver-Sharpey), Sir Kenneth Clark (Lloyd-Roberts), J. F. Brock (Humphry Davy Rolleston), all for 1959; D. E. Denny-Brown (Croonian), K. D. Keele (Fitzpatrick), F. R. Bettley (Watson Smith), J. W. Crofton (Marc Daniels), for 1960.

The following, having satisfied the censors' board, were admitted to the membership:

Chrystal H. Ashton, B.M. Oxon., G. V. Balmforth, M.B. Lond., J. L. T. Birley, B.M. Oxon., D. F. Cappell, C.B.E., M.D. Glasg., J. R. Curtis, M.B. Lond., C. T. Dollery, M.B. Birm., E. B. D. Dowdle, M.D. Cape Town, D. W. Evans, M.B. Wales, K. F. Fairley, M.D. Melb., O. W. Hill, M.B. Cantab., W. B. Jackson, M.B. N.Z., J. V. Jones, B.M. Oxon., N. F. Jones, M.B. Cantab., H. R. Klein, M.B. Witwatersrand, B. E. Lovelace, M.B. Lond., M. W. McNicol, M.B. Glasg., Victor Parsons, B.M. Oxon., Dorab Jehangir Patel, M.B. Bombay, J. S. Penington, M.D. Melb., B. W. B. Penman, M.B. Edin., E. V. Pieris, M.B. Ceylon, Alan Pollard, M.B. Cantab., D. H. H. Pullon, M.B. N.Z., A. M. Rankin, M.B. Adelaide, M. D. Readett, M.B. Birm., J. L. Reed, M.B. Cantab., Shelagh M. Richards, M.B. Sheff., Chava E. Rotem, M.D. Lausanne, H. H. Shawdon, M.B. Cantab., C. K. Simpson, M.D. Lond., J. G. Sloman, M.B. Melb., M. A. Smith, B.M. Oxon., A. E. Stevens, M.B. Lond., D. J. Stoker, M.B. Lond., M. W. Swallow, M.B. Lond., A. K. Thould, M.B. Lond., G. E. G. Williams, M.B. Cantab., I. V. Wilson, M.B. Durh., John Wilson, M.B. Durh., Susannah M. Woodcock, M.B. Lond., K. J. Zilkha, M.B. Lond.

Licences to practise were conferred on the following 125 candidates who had passed the final examination of the Conjoint Board:

A. R. Adamson, Richard Allaye, A. J. R. Anderson, A. L. Ansdell, J. T. Aroney, J. S. Bailey, Ekundayo Abayomi Bamgboye, Jehangir Edalji Banatvala, M. D. Begley, L. S. Bernstein, W. H. Bevan-Thomas, G. A. Bewley, W. M. Bodger, P. R. Brass, R. C. Bretday, P. D. G. Briggs, F. H. Brindle, M. H. Brooke, F. T. Brough, M. H. Bull, R. W. Burt, L. J. Burton, W. D. Callum, I. G. Carnegie Brown, I. G. Christie, P. W. Clements, D. L. Common, Daniel Connan, Edith M. Cooke, J. C. Couve de Murville, P. A. Cullum, T. O. Dada, Pauline M. H. Davidson, N. A. De Heer, Edna M. Dunn, A. J. Earl, R. J. Earlam, D. J. Ellam, R. C. Evans, R. J. Evans, R. E. Fallowfield, Martin Fisher, H. J. L. Francis, Paul Fursdon, H. A. Garfinkel, P. B. Garland, P. M. Gelpke, J. M. Goyder, John Grant, R. S. Greenwood, J. S. Grimshaw, A. C. Halliwell, J. D. Hardcastle, D. C. Harvey, A. L. Hovenden, Anne T. Irvine, Anne Jacques, Sadrudin Alibhai Janmohamed, I. N. L. Johnston, Jane M. Jones, Winifred N. Kaine, N. B. Kirkland, Hilda Koilpillai, Leslaw Kwasny, Andrea M. D. Langford, Reza Larizadeh, N. K. Leiper, D. W. Lewis, C. M. Liassides, P. O. Liebling, Maxwell Lindsay, Marion E. Liss, T. A. Lloyd-James, A. M. Lush, D. B. Macadam, B. J. T. McAvoy, C. E. Macdonald, J. W. Mack, K. V. Mellor, David Mercer, A. R. Molyneux, Pauline S. Monro, H. G. Morgan, George Moses, I. S. Muir, Muhammad Yacoub Najjar, A. I. Nwabueze, N. W. Oakley, Kolawole Adeniyi Olafimihan, E. O. Olurin, S. B. Oni, B. A. Oni-Okpaku, E. H. Osborn-Smith, J. D. Owen, Glenys R. Packer, N. D. Parkin, M. G. O. Parrish, Bruce Pitt-Payne, D. Powell, J. N. Powell, E. B. Raftery, M. J. Ramsden, D. J. Richards, J. M. R. Ridley, Raj Kishore Saksena, Nanju Sankarayya, M. A. Sasson, D. C. L. Savage, Montague Segal, R. I. D. Simpson, Margaret R. Skelton, B. R. T. Smith, J. M. Stephenson, J. M. Taylor, Geraldine Thomas, J. B. Traherne, W. J. Trowell, G. L. Tullett, Fidelis Nwankwo Udeh, A. C. Upjohn, Sri Krishna-Cumar Rajakesari Villavarayan, Daphne M. Ward, P. H. Waterfield, W. F. Whimster, Richard Yeo.

Diplomas were conferred jointly with the Royal College of Surgeons of England on the following:

D.A.—Kamal Chandra Agarwala, Abdul Amir Alwan Al-Uzri, Bantwal Raghavendra Baliga, F. E. Bennetts, E. P. Berwick, F. R. Bhupalan, Maryrose E. Brewerton, Peter Brine, E. F. Brooks, Georgina D. Brown, T. H. L. Bryson, J. G. Camilleri, W. F. Carpenter, Gerald Cartmel, Pamela Channon, F. B. N. Clarke, A. J. Clement, Elmer Clissold, B. J. H. H. Colback, C. F. Conway, Marian H. Dadaczynski, J. P. Davie, I. B. Denny, G. R. Dow, Thomas Dowell, A. J. F. Eberle, N. L. Edmond, H. J. Ellis, Myrtle Farquharson, E. L. Fischer, Frank Fisher, Freda W. Fleming, J. W. Gammie, Deb Narayan Ganguly, M. A. Gilbert, Heath P. Gillespie, G. B. Gillett, J. A. M. Goodwin, B. G. H. Grant, Ajoy Gupta, Marcus Haase, R. L. Hargrove, Pamela A. Harris, Sylvia K. Hepton, Eric Holmes, Bridget A. Jepson, H. W. F. Jones, Margaret L. L. Jones, Olive C. Jones, Syed Ahmed Kabir, Karingan Ranganath Kamath Norman Kaplan, Shafiquddin Ahmed Khan, P. F. Knight, R. F. Knight, J. R. Lawrance-Owen, M. G. Leonard, R. N. Lewis, J. G. Lindsay, J. H. L. Lloyd-Thomas, J. N. Lunn, A. J. McDonald, Hugh McIntyre, T. D. M. McNeill, Frances M. McQuitty, S. W. McVicker, John Mackett, R. E. Maclaurin, H. A. Maher, I. M. J. Mair, Ma Shu Poh, Kamil Mustafa, Manohar Laxman Nene, B. E. Ohmacht, G. D. Parbrook, Dawood Ahmed Patelle, Audrey M. Peeling, P. A. Pelham, Margaret E. Pickering-Pick, W. M. Pillow, Lora Y. Pratt, P. B. W. Price, Denis Proctor, Arnold Rieck, Brenda K. Rimmer, R. S. Ritchie, Pamela D. Roberts, Anna I. Robertson, Sheila J. B. Robertson, R. H. Robinson, David Saltoun, Betty V. Scott, R. O. Selby, H. W. Stark, J. G. Thomson, L. G. von Thomann, Alice van Waterschoodt, H. J. White, Anne M. Wilson, G. R. V. Worrall, P. R. Wykes, Ming-Hon Yeung, Roman Zeeher.

D.C.H.—J. T. Binless, D. G. Cottom.

D.I.H.—P. G. Cannon, Jayanta Kumar Chakravarti, A. J. Hibell, P. G. W. A. Lommerse, H. F. McElligott, Manzur Ahmad Malik, A. C. Reith, Maung Myo Tint, J. de M. Vink.

D.L.O.—Lajpat Rai Aggrawal, Badiul Alam, A. A. Anderson, P. J. Batchelor, P. G. A. Bloomer, R. C. Bloomfield, J. T. Buffin, R. M. C. Butler, Shroff Rama Setty Chandrasekhar, G. W. S. Choa, M. G. Cox, T. J. Crowe, C. E. Gabriel, Dwijendar Prosad Ghosh, D. J. Godfrey, A. N. Gorshenin, Rameshwar Lal Gupta, P. C. Leeson, Brian Livesey, M. B. Stanton, Brenda L. Stather-Dunn, J. B. Walker.

D.M.R.D.—Walimuni Wilson Mendis Abeysekera, D. M. Alexander, Tara Pade Banerjee, D. M. Brebner, P. M. Bretland, J. A. D. Briggs, F. K. Downsbrough, H. E. Engelbrecht, I. H. Lawrence, K. M. Mayo, J. G. A. Monks, Asok Kumar Mukhopadhyay, R. M. Murray-Leslie, Belgod Krishnaiyengar Narasimha Murthy, Krishnar Pasupathy, E. J. Pick, R. G. Pitman, D. H. Provan, J. F. Ryan, Muriel E. Sidaway, William Wilson, F. W. Wright.

D.M.R.T.—Prabhatendu Banerjee, J. S. Bunting, J. C. McI. Fetterly, G. A. L. G. Glazebrook, Nikolaos Halazonetis, Norman MacLeod, Dorothy S. Murrell, Sumanaweera Nissanga, T. A. O'Donnell.

D.O.—D. E. P. Jones.

D. Path.—Thomas Gordon, Charles Isaacson, Hugh Richmond, T. G. Scott, Dilip Kumar Sen, Geoffrey Taylor, Poothathamby Thillainathan, C. A. H. Trench.

D.P.M.—H. A. Anderson, Margaret L. Arden, J. K. Binns, Asuncion F. Cheyne, Marion B. Coleman, Mary J. Collins, G. E. Cook, Harutiun Davidian, Margaret McC. Dewar, David Duncan, R. L. Duncan, J. P. Farrell, P. G. Fawcett, K. M. Fraser, Pearl Goddard, H. S. Greer, J. G. Hegarty, I. A. Horton, L. C. Hurst, Muhammad Said Rasem Kamal, K. E. Le Page, Jeremy Lister, E. B. McDowall, Agnes M. McGlashan, L. E. McLoughlin, Beryl Margolis, Robert Middlefell, Helen M. P. Molony, J. S. V. Mouat, E. W. P. Noall, D. P. Oakley, R. H. V. Ollendorff, H. I. H. Porcher, S. G. Rowe, Allan Sinclair, F. G. Spear, Alexander Stevenson, M. H. Sunderland, E. L. Sutherland, R. P. M. Urquhart, P. K. G. Warren, J. M. Woodforde, A. R. Worters, W. B. Wright.

D.P.H.—Grace V. Andrew, Abdul Wahab Bin Mohamed Ariff, Rosemary A. Begg, J. T. Cecil, G. F. Devey, Sheila H. E. Fairweather, Renato Gracias, Charles Harris, V. A. Lloyd, Mahmoud Hussein Mahmoud, R. G. Newberry, R. A. Ryan, Ziyauddir Qamaruddin Shaikh, J. B. Stafford, A. W. Tranter, John Waters.

Royal College of Surgeons of England

At a meeting of the council on July 31, with Sir James Paterson Ross, the president, in the chair, Sir Reginald Watson-Jones, Prof. D. M. Douglas, and Mr. W. A. Mill were elected members of the court of examiners.

Lieut.-Colonel R. H. Robinson, R.A.M.C., was awarded the Mitchiner medal, Wing-Commander W. B. Thorburn the Lady Cade medal, and Surgeon Commander W. E. Crocker, R.N., the Gilbert Blane medal.

A diploma of fellowship was granted to Padmanahden Narendran.

Diplomas and licences to practise were conferred jointly with the Royal College of Physicians on those named above.

Society for Applied Bacteriology

The following officers have been elected:

President, Mr. D. A. McKenzie; hon. secretary, Mr. G. Sykes (Boots Pure Drug Co. Ltd., Microbiology Division, Standards Department, Nottingham); hon. treasurer, Mr. G. Elis Jones; editor-in-chief, Dr. S. E. Jacobs; editor, Dr. C. A. E. Briggs; hon. publications manager, Mr. A. H. Walters; hon. advertising manager, Mr. E. J. Mann; committee, Dr. Eve Billing, Prof. E. L. Crossley, Dr. J. G. Davis, Dr. N. R. Knowles, Dr. Jane Meiklejohn, Mr. C. A. Scarlett, and Dr. M. Woodbine.

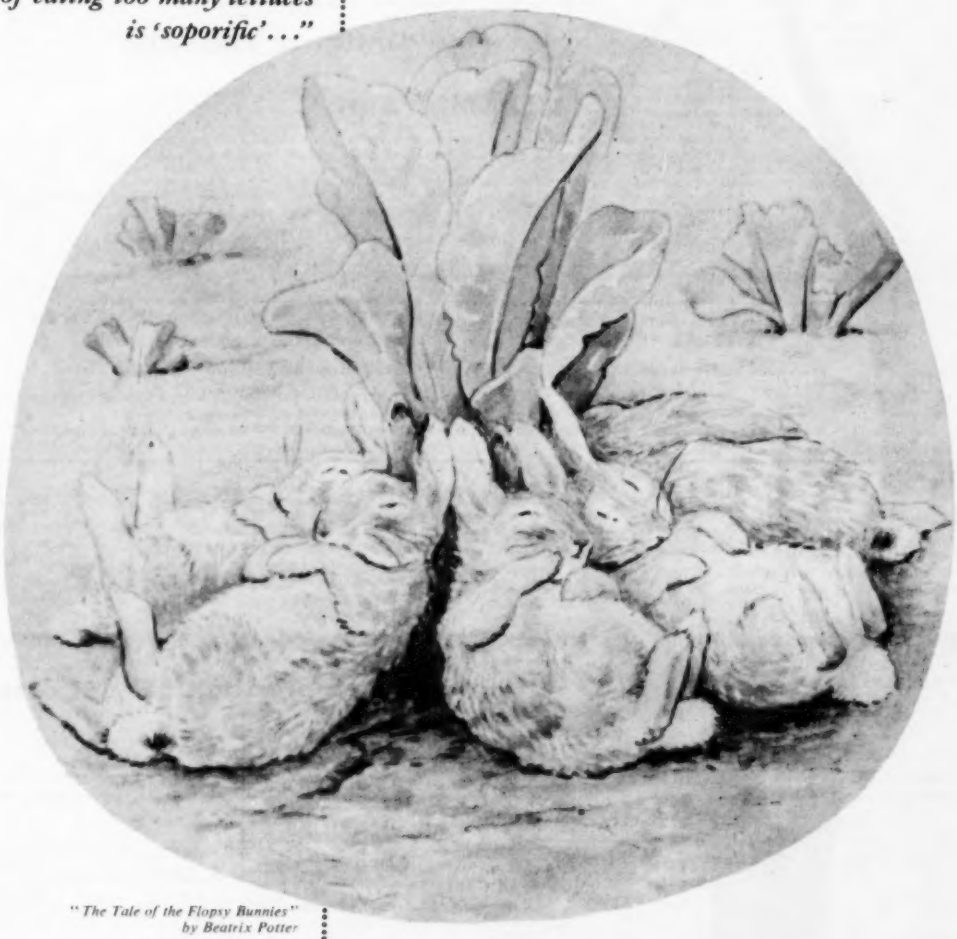
Isaac Wolfson Foundation

Since this Foundation was started in 1955 it has distributed £1,114,000. Its latest gifts include £250,000 to the Westminster Hospital School of Nursing and £25,000 to the British Council for the Welfare of Spastics to build residences and workshops at Beaconsfield.

The policy of the Foundation, which has a capital fund of more than £6 million, is to advance education and health in the United Kingdom and Commonwealth with particular reference to "scientific and technological education, building facilities for higher education, youth activities, general medical research, cancer research, and medical, surgical, and nursing services". The board of trustees includes Sir Stanford Cade and Lord Evans.

Surgeon Captain C. B. Nicholson has been appointed an honorary surgeon to the Queen in succession to Surgeon Rear-Admiral E. T. S. Rudd.

"It is said that the effect of eating too many lettuces is 'soporific'..."



"The Tale of the Flopsy Bunnies" by Beatrix Potter

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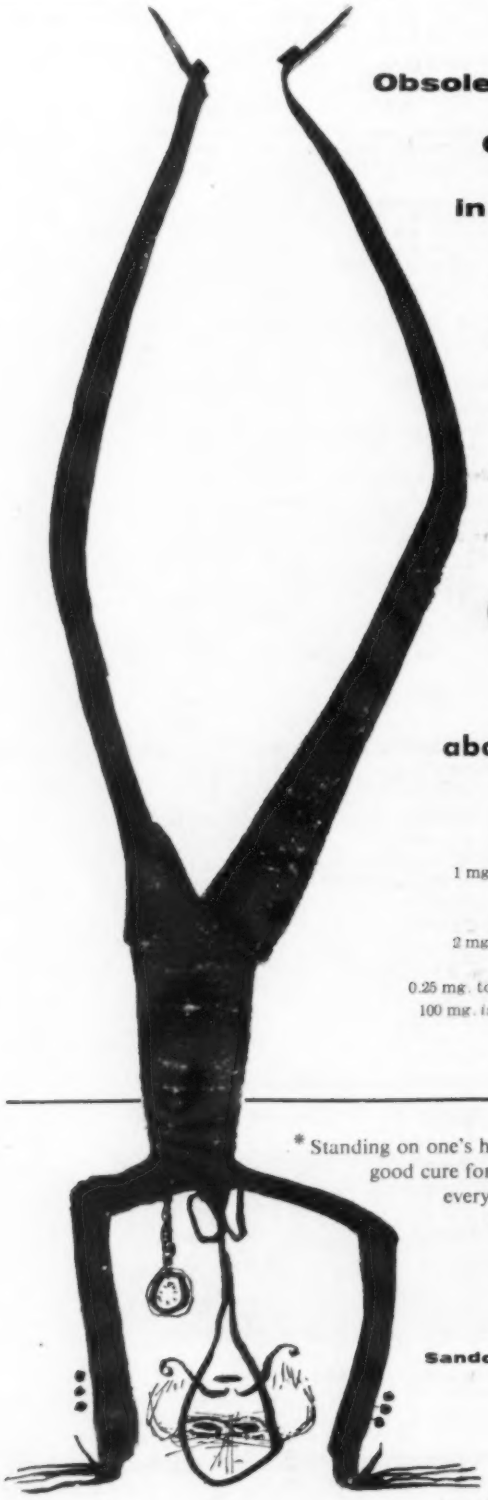

Obsolete

Gravitational Therapy

in Migraine

"You are old, Father William," the young man said,
"And your hair has become very white;
And yet you incessantly stand on your head—
Do you think, at your age, it is right?"

"In my youth," Father William replied to his son,
"I did it to cure the migraine;*
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And take Cafergot when I'm in pain."

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* Standing on one's head is reputed to be a good cure for migraine[1]—but not every patient is so agile.

[1] *Brit. med. J.* (1957) 2, 633

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MEDICAL SUPERINTENDENT: THOMAS TENNENT, M.D., F.R.C.P., D.P.H., D.P.M.

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A 2-week COURSE OF LECTURES, DEMONSTRATIONS AND TUTORIALS for postgraduates preparing for higher diplomas in anæsthetics will be held from 13TH to 24TH OCTOBER, 1958.

Fees: Lectures and demonstrations £15 15s.
Tutorial discussion groups £10 10s.

Further details and application forms may be obtained from Mr. W. F. DAVIS, Secretary, Faculty of Anæsthetists, Royal College of Surgeons of England, Lincoln's Inn-fields, London, W.C.2 (Telephone HOLborn 3474, extension 23).

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A Refresher Course of 1 week's duration, designed for general practitioners, will be held at the Victoria Infirmary, Langside, Glasgow, S.2, from 22ND to 27TH SEPTEMBER, 1958. The course will consist, so far as possible, of bedside discussions and clinical conferences. Sessions will deal with general medicine, including cardiology and hæmatology, general surgery, orthopædics, gynæcology, ophthalmology, dermatology, and urology.

Lunch will be available at the Hospital.

The Course will rank for Government grant to eligible National Health Service practitioners. The fee for practitioners not claiming Government grant is £5 5s.

Since the number of places is limited, those wishing to attend should make early application to the Director of Postgraduate Medical Education, The University, Glasgow, W.2, from whom further information may be obtained.

POSTGRADUATE COURSE IN ORTHOPÆDIC SURGERY

to be held at

HARLOW WOOD ORTHOPÆDIC HOSPITAL, near MANSFIELD, NOTTINGHAMSHIRE

27TH–31ST OCTOBER, 1958 (inclusive)

27TH OCT.	The Treatment of Talipes Equinovarus	Mr. S. A. S. MALKIN, C.B.E.
	Foot Problems in Childhood	Mr. W. WAUGH
	Causes and Treatment of Delayed-union and Non-union in Fractures of Long Bones	Mr. E. A. NICOLL, C.B.E.
28TH OCT.	The Sequelæ of Poliomyelitis	Mr. W. J. SHARRARD
	Some Problems of Severe Limb Injuries	Mr. A. N. BIRKETT
	Hand Surgery	Mr. R. G. PULVERTAFT, Mr. D. A. C. REID
29TH OCT.	Hand Surgery	Mr. R. G. PULVERTAFT, Mr. D. A. C. REID
	Osteoarthritis of the Hip	Mr. J. P. CAMPBELL, Mr. J. D. MALLOCH
30TH OCT.	The Causes of Low Back Pain and its Treatment	Mr. E. W. O. ADKINS
	Surgery of Rheumatic Diseases	Mr. L. MORRIS
	Tuberculosis of the Hip	Mr. J. P. JACKSON
	Diagnosis and Treatment of Paraplegia	Dr. A. G. HARDY, M.B.E.
31ST OCT.	Lumbo-sacral Instability as a Cause of Backache	Dr. J. HILL (Durban, South Africa)
	The Early Diagnosis of Spinal Cord Injuries	Mr. F. W. HOLDSWORTH
	Arthodesis of the Hip by Central Dislocation Technique	Mr. J. CHARNLEY (Manchester Royal Infirmary)
	The Causes and Treatment of Cervical Pain	Mr. H. OSMOND-CLARKE, C.B.E. (London Hospital)

No fee for the Course.

Applications to be sent to the Secretary, Harlow Wood Orthopædic Hospital. Limited accommodation available, if required, at associated Hospital.

L.M.S.S.A.

FINAL EXAMINATION: MEDICINE and SURGERY, 11th August, 13th October, 10th November, 1958. MIDWIFERY and PATHOLOGY, 12th August, 14th October, 11th November, 1958. MASTERY OF MIDWIFERY, May and November. DIPLOMA in INDUSTRIAL HEALTH, July and December.

For regulations apply REGISTRAR, Apothecaries Hall, Black Friars-lane, London, E.C.4.

THE UNIVERSITY OF MANCHESTER. Applications are invited for the post of SURGICAL TUTOR. Salary £1050 p.a. with membership of Children's Allowance Scheme. The Tutor will be required to give instruction in practical surgery and supervise the studies of students during their period of clinical apprenticeship. In addition the Tutor will be required to take part in the clinical and research activities of the Department of Surgery. A higher qualification in surgery will be considered an advantage.

Applications should be sent not later than 16th August to the Registrar, the University, Manchester, 13, from whom further particulars and forms of application may be obtained.

NEWCASTLE REGIONAL HOSPITAL BOARD. GERIATRIC UNIT, GENERAL HOSPITAL, SUNDERLAND. NUFFIELD RESEARCH FELLOWSHIP for Clinical Research Into Problems of Ageing. Whole-time appointment for 1 year initially. Salary £1061 10s. Previous experience of research desirable but not essential.

Applications, with names and addresses of 2 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

UNIVERSITY OF GLASGOW

LECTURESHIP IN MATERIA MEDICA

Applications are invited for appointment to a LECTURESHIP IN MATERIA MEDICA combined with a clinical post in the wards, in the charge of the Professor, at Stobhill Hospital. The total salary attached to the post will be made up of half the salary on the appropriate University scale for Clinical Lecturers and half the salary on the National Health Service scale appropriate to the successful candidate's grading.

Applications (12 copies) should be lodged, not later than 29th August, 1958, with the undersigned, from whom further particulars may be obtained.

ROBT. T. HUTCHESON, Secretary of the University Court.

UNIVERSITY OF DURHAM. MEDICAL SCHOOL, KING'S COLLEGE, NEWCASTLE UPON TYNE, and the UNITED NEWCASTLE UPON TYNE HOSPITALS. The Council of King's College invite applications for the post of FIRST ASSISTANT in the Joint Department of Psychological Medicine, Medical School, and the Royal Victoria Infirmary, Newcastle upon Tyne. Candidates should hold a Diploma in Psychological Medicine or its equivalent and preferably a higher qualification in General Medicine. The successful candidate will work under the direction of the Professor of Psychological Medicine and will be expected to take part in both undergraduate and postgraduate teaching and to undertake research. He will also be expected to carry out clinical duties in the Teaching Hospital and in the Joint University and Hospital Department at the Newcastle General Hospital. The Department is closely associated with the local Mental Hospital (1150 Beds) for teaching and research purposes. Salary within the range £1400–£1900 p.a. with superannuation benefits and family allowance. Duties to commence 1st October, 1958, or as soon as possible thereafter.

Further particulars may be obtained from the undersigned, to whom applications (12 copies) should be addressed so as to reach him not later than Wednesday, 27th August, 1958.

G. R. HANSON, Registrar of King's College.

UNIVERSITY OF WALES (The Welsh National School OF MEDICINE). It is proposed to appoint an ASSISTANT MEDICAL OFFICER (Male) to the University of Wales Student Health Service in the grade Assistant Lecturer (medical) (scale £900–£100–£1250). The appointed Medical Officer will work principally in the University College of Wales, Aberystwyth and North Wales, Bangor, and will be expected to reside in Aberystwyth. This is an appointment offering interesting work including opportunities for research.

Applications should be made within 3 weeks of the appearance of this advertisement to the Secretary, The Welsh National School of Medicine, 34, Newport-road, Cardiff, from whom further particulars can be obtained.

UNIVERSITY OF MALAYA. Applications are invited for (*a*) LECTURESHIP or (*b*) ASSISTANT LECTURESHIP IN PHARMACOLOGY. Salary scales: for medically qualified candidates (*a*) £1295–£49–£1442/£1540–£56–£1988 p.a., (*b*) £1148–£49–£1246 p.a. For non-medically qualified candidates (*a*) £1148–£49–£1442/£1540–£56–£1820 p.a., (*b*) £1001–£49–£1099 p.a., entry-point determined by qualifications and experience. Allowances: expatriation in range £280–£308 p.a., cost-of-living in range £210–£560 p.a. Passages for appointee, wife, and children under 12 years. Part-furnished quarters at reasonable rent. Provident fund scheme.

Detailed applications (6 copies), naming 3 referees, by 15th September, 1958, to Secretary, Inter-University Council for Higher Education Overseas, 29, Woburn-square, London, W.C.1, from whom further particulars may be obtained.

Hospital Services: Senior Appointments

BETHLEM ROYAL HOSPITAL AND THE MAUDSLEY HOSPITAL. The Board of Governors invite applications from psychiatrists of requisite qualifications for the post of PHYSICIAN, to attend on 3 sessions a week. The post is of Consultant status. An Honorary Consultant who is at present carrying out the duties of the post is an applicant for it.

Applications (10 copies), giving curriculum vitæ and the names of 3 referees, should be sent to K. J. JOHNSON, House Governor and Secretary, The Maudsley Hospital, Denmark Hill, S.E.5, within 1 month of appearance of this advertisement.

LONDON CLINIC. (164 Beds.) Applications are invited for the post of DIRECTOR of the Department of Pathology. Applicants must be registered medical practitioners with a wide experience in pathology. The successful candidate will be required to join a contributory superannuation scheme if not already a member. There will be ample security of tenure of the appointment. The total emoluments will depend on qualifications and experience, but will not be less than £4000 p.a., rising to £5750 p.a.

Applications, stating age, qualifications and details of past and present appointments, together with the names of 3 referees, should be forwarded to the Secretary, London Clinic, Devonshire-place, London, W.1.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Part-time CONSULTANT SURGEON (7 notional half-days weekly), City General Hospital, Stoke-on-Trent. Higher qualification and wide experience specialty essential.

Applications (15 copies), stating age, qualifications, nationality, present and previous appointments and details of 3 referees, to Secretary, 10, Augustus-road, Birmingham, 15, by 8th September.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. Locum CONSULTANT OBSTETRICIAN AND GYNÆCOLOGIST, Peterborough Group of hospitals, from 8th September to 30th November, 1958. Possible extension beyond this date pending appointment of additional Consultant.

Applications, stating age, experience and names of 3 referees, to the Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

Enfield War Memorial Hospital

Part-time CONSULTANT SURGEON for 1 session a week (outpatient and operating).

Chelmsford Group of Hospitals

Maximum Part-time CONSULTANT SURGEON; duties mainly at Chelmsford and Essex Hospital and St. John's Hospital, Chelmsford. Residence in area is a condition of appointment. Further particulars on application.

Tottenham, Central and Hackney Groups of Hospitals

Whole-time ASSISTANT in Physical Medicine (Senior Hospital Medical Officer grade). Duties at The Prince of Wales's General Hospital, N.15, and other hospitals in the Tottenham Group (6 sessions), St. Leonards (N.1), and Bethnal Green (E.2) Hospitals (2 sessions), and Hackney (E.9) and The German (E.8) Hospitals (3 sessions).

Applications (5 copies each for surgical posts and 7 for physical medicine post), and names of 3 referees, should reach the Secretary, 11A, Portland-place, London, W.1, by Saturday, 6th September, 1958.

ROYAL FREE HOSPITAL, Gray's Inn-road, W.C.1. Applications are invited from registered medical practitioners for the post of Part-time DIRECTOR of Diagnostic Radiology. Applicants must hold the Diploma in Medical Radiology, and possession also of a higher qualification is desirable.

Applications, giving details of qualifications and experience, together with the names of 3 referees, should be sent to the Secretary to the Board of Governors not later than 6th September, 1958.

LEEDS REGIONAL HOSPITAL BOARD. Applications are invited for appointment of Maximum Part-time CONSULTANT in General Medicine for duties at the Harrogate General and other hospitals in the Harrogate and Ripon Group. Successful candidate will be required to reside in Harrogate and also to devote 2 sessions entirely to Geriatric work. Cardiological experience an advantage.

Applications (12 copies), stating age, qualifications and details of present and previous appointments with dates, and names and addresses of 3 referees, to the Secretary, Park Parade, Harrogate, by 15th September, 1958.

LEEDS REGIONAL HOSPITAL BOARD. Locum CONSULTANT in Ophthalmology (whole-time) for duties in Leeds and Harrogate. The post will be vacant in September and the appointment will be for approximately 3–4 months.

Applications, stating age, qualifications, details of appointments held showing dates, with the names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, by 30th August, 1958.

MANCHESTER REGIONAL HOSPITAL BOARD. Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer), Prestwich (Mental) Hospital, Manchester (about 3000 Beds). Single person can be accommodated in Hospital, otherwise post non-resident. All modern forms of treatment are undertaken. Candidates should have had wide experience in psychiatry; D.P.M. desirable.

Application forms from the Senior Administrative Medical Officer to the Board, Cheetwood-road, Manchester, 8, to be returned by 20th August, 1958.

NEWCASTLE REGIONAL HOSPITAL BOARD. Special AREA OF CUMBERLAND AND NORTH WESTMORLAND. ANÆSTHETIST (Consultant), whole-time or maximum part-time, for East Cumberland Group of hospitals, to commence on 1st January, 1959. Main hospitals, Cumberland Infirmary, Carlisle (340 Beds), and City General Hospital, Carlisle (180 Beds). Appointee required to reside in or within 5 miles of Carlisle.

Applications, together with names of 1 to 3 referees, to Senior Administrative Medical Officer, 72, Warwick-road, Carlisle, within 28 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. Senior CASUALTY OFFICER, whole-time, for North Tees-side Group of hospitals—main hospital Stockton and Thornaby (130 Beds). Duration of tenure of post not exceeding 4 years. Salary within range £1653 15s.–£2126 5s. or £1548 15s.–£2126 5s. Appointee will be required, subject to the supervision of the Senior Surgeon to General Surgical Clinic No. 3 and the Senior Orthopædic Surgeon, to organise work of the busy Casualty Department. Accommodation near hospital available. Further particulars from Senior Surgeon, General Surgical Clinic No. 3, Stockton and Thornaby Hospital, Stockton-on-Tees.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of Locum Whole-time OPHTHALMOLOGIST (Senior Hospital Medical Officer grading) required immediately at the Glasgow Ophthalmic Institution for a period of 12–18 months.

Applications, with details of age, qualifications, experience, present appointment, and the names of 3 referees, to the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the whole-time appointment of CONSULTANT PSYCHIATRIST at Bexley Hospital, Dartford Heath, Bexley, Kent. Accommodation is available for an unmarried practitioner only. Candidates should possess a D.P.M. and preferably a higher qualification; psychiatric hospital and outpatient clinic experience is essential, and candidates should also have had experience in modern psychiatric therapeutic procedures, including psychotherapy and occupational therapy. Applicants may visit the hospital.

Applications, stating nationality, age, sex, qualifications and experience, including details of present appointment and of war service, together with the names and addresses of 3 referees, to be sent to the Secretary, Advisory Appointments Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 23rd August, 1958.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited to fill a vacancy for a Whole-time CONSULTANT PSYCHIATRIST to the St. Francis and The Lady Chichester Group of hospitals, for duty at St. Francis Hospital, Haywards Heath, Sussex, and in the Neuropsychiatric Unit at Hurstwood Park. Duties will include visits to the Observation Wards at Brighton. The successful applicant will be required to reside within reasonable distance of the Hospital. Candidates should possess a D.P.M. and a higher medical qualification; psychiatric hospital and outpatient clinic experience is essential, and candidates should have had experience in modern psychiatric therapeutic procedures, including psychotherapy and occupational therapy. Applicants may visit the hospital.

Apply, stating nationality, age, sex, qualifications and experience, including details of present appointment and of war service, together with the names and addresses of 3 referees, to the Secretary, Advisory Appointments Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 23rd August, 1958.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires CONSULTANT CHEMICAL PATHOLOGIST (whole-time or maximum part-time) in the Chichester Group of hospitals and Graylingwell Hospital. Candidates should have some general knowledge of clinical pathology and morbid anatomy, but will be required to take charge of all chemical pathology in the area. Post vacant January, 1959.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, London, W.1, by 6th September, 1958. Applicants may visit laboratories in the area by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time ASSISTANT PATHOLOGIST (Senior Hospital Medical Officer grade) for the Kingston (Surrey) Group Laboratory. Principal duties will be in haematology, but experience in bacteriology will be an advantage. Duties include visits to hospitals in the Group. The Laboratory offers very wide experience and opportunities for research in clinical pathology. Post vacant January, 1959.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, London, W.1, by 8th September, 1958. Applicants may visit Laboratory by arrangement with Group Pathologist.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time SENIOR ASSISTANT PSYCHIATRIST required at the Towers Hospital, Leicester. Salary scale £1653 15s.–£52 10s.–£2126 5s. p.a.

Application form and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 6th September, 1958.

CANADA. UNIVERSITY OF ALBERTA HOSPITAL, EDMONTON, ALBERTA, CANADA. Applications are invited for the position of ASSISTANT DIRECTOR of the Department of Clinical Laboratory Services. The duties will be concerned with the future development of the biochemistry laboratory service in the Hospital, consulting and advising on clinical problems and research projects involving biochemistry and teaching. A teaching appointment in the University of Alberta Medical School, while not automatic with this appointment, is customary. There will be ample opportunity to carry on individual research. The qualifications required are a degree in medicine and special training and experience in biochemistry. Preference will be given to those holding the M.R.C.P. or F.R.C.P., or a doctorate degree in biochemistry. Male, age 30–40, preferred but not essential. Salary $10,000–$12,000 p.a. Further details may be obtained from Professor E. J. King, Postgraduate Medical School, Ducane-road, W.12, London, England.

Interested parties should apply to the Medical Superintendent, University of Alberta Hospital, giving full details and the names of 2 referees.

CANADA. WESTERN NOVA SCOTIA CLINIC. Applications are invited for the post of ASSISTANT PSYCHIATRIST at a Government-supported rural clinic in Nova Scotia. The appointment is for 1 year in the first instance, but may be extended by mutual agreement on completion of this period. Interest in community and preventive psychiatry is essential and preference will be given to candidates possessing the D.P.M. Salary $8700 p.a.

Further particulars from the Director, Western Nova Scotia Clinic, P.O. Box 249, Digby, Nova Scotia, Canada.

NAIROBI. THE AGA KHAN HOSPITAL. Applications are invited for the whole-time post of PHYSICIAN, with experience in pædiatrics and tropical diseases. Salary at the rate of £2500 p.a.; not more than 5% being deducted for house and basic furniture. 2-year contract, renewable. Superannuation provided for. Local leave annually. Passage paid out, and home at end of contract. This new Hospital in Nairobi is due to open on 8th September with at first 120 Beds. Plans exist for developing the Hospital as a multi-racial medical centre.

Applications, with the names of 2 referees, to be sent, not later than 20th August, to R. G. A. BEAUMONT, Secretary, Aga Khan Hospital, c/o St. George's Hospital, London, S.W.1.

SOUTH AUSTRALIA. THE QUEEN VICTORIA MATERNITY HOSPITAL INC., 22, Victoria-avenue, ROSE PARK, SOUTH AUSTRALIA. Applications are invited for the position of ASSISTANT MEDICAL SUPERINTENDENT of the above Hospital. The appointment will be initially for a period of 12 months with provision for renewal subject to satisfactory service. Applicants must either be Members of the Royal College of Obstetricians and Gynæcologists or have had a minimum of 12 months' experience in an obstetric teaching hospital. Salary will be within the range of £A1575–£A2203 p.a., the initial figure being dependent on qualifications and experience.

Applications in writing, comprising full personal details, particulars of experience, and copies of 3 testimonials, are to be in the hands of the undersigned by 22nd September, 1958.

V. R. ATKINSON, Secretary/Manager.

Hospital Services: Junior Appointments

CONNAUGHT HOSPITAL, Walthamstow, E.17. Locum RESIDENT ANÆSTHETIST (Senior House Officer) required from 18th August to 1st September.

Apply Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

CONNAUGHT HOSPITAL, Walthamstow, E.17. Locum CASUALTY OFFICER (Senior House Officer) required from 18th August to 8th September.

Apply Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

DULWICH HOSPITAL (in association with King's College Hospital Medical School for teaching purposes), East Dulwich-grove, S.E.22. HOUSE OFFICER (general surgical duties) required from 20th August. Recognised pre-registration post.

Applications, with copy testimonials or names of 2 referees, to Group Secretary, Camberwell Hospital Management Committee, Dulwich Hospital.

FOUNTAIN GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR REGISTRAR or REGISTRAR required for duty in the above Group which comprises some 800 Beds for mental deficiency, mainly for children. There is an Outpatient Department and a considerable amount of teaching and research is done. Possession of D.P.M. is essential for appointment in the Senior Registrar grade. Experience of children's diseases is an advantage. Candidates may visit the Hospital.

Application forms and further details from Secretary, Fountain Hospital, Tooting-grove, London, S.W.17. Completed forms should reach the Secretary by 22nd August, 1958.

GERMAN HOSPITAL, London, E.8. (General, 157 Beds.) Applications for the 6-month resident post, vacant 5th September, of HOUSE SURGEON (obstetrics and gynæcology) should reach the Group Secretary, Hackney Hospital, London, E.9, by 18th August, quoting GH HSO.

GUY'S HOSPITAL, S.E.1. Applications are invited for the post of REGISTRAR (mid-grade) in the Department of Dermatology, with duties from 1st October, 1958, until 30th September, 1959, in the first instance. It is desirable that applicants should be in possession of the M.R.C.P.

Forms of application are obtainable from, and should be lodged with, the Superintendent, Guy's Hospital, London Bridge, S.E.1, not later than 21st August, 1958.

GUY'S-MAUDSLEY NEUROSURGICAL UNIT. Applications are invited for the resident post of SENIOR HOUSE OFFICER for 6 months commencing on 1st October, 1958. The Unit, which is housed in the Maudsley Hospital, serves both Guy's Hospital, and the Bethlem Royal Hospital and the Maudsley Hospital.

Applications should be made within 2 weeks of the appearance of this advertisement to K. J. JOHNSON, House Governor and Secretary, Maudsley Hospital, Denmark Hill, S.E.5.

HAMMERSMITH HOSPITAL AND INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY, Ducane-road, London, W.12. RESIDENT HOUSE SURGEON (obstetrics) required 1st October. Recognised for M.R.C.O.G.

Detailed applications, copies 2 recent testimonials, to Secretary, Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, by 18th August.

HIGHLANDS GENERAL HOSPITAL, Winchmore Hill, N.21. HOUSE SURGEON for Gynæcology and General Surgery.

Applications, with copies of 3 testimonials and name and address of 1 referee, to Hospital Secretary.

HIGHLANDS GENERAL HOSPITAL, Winchmore Hill, N.21. HOUSE SURGEON (Senior House Officer grade) required. Duties mainly orthopædic, some E.N.T. and emergency general surgery. New operating-theatre. Outpatient and Casualty Department.

Applications, with copies of 3 testimonials and name and address of 1 referee, to Hospital Secretary.

HIGHLANDS GENERAL HOSPITAL, Winchmore Hill, N.21. HOUSE PHYSICIAN vacant 13th August, 1958. Preference given to applicants seeking pre-registration post under Medical Act, 1950.

Applications, with copies of 3 testimonials and name and address of 1 referee, to Hospital Secretary.

MARIE CURIE HOSPITAL, 66, Fitzjohn's-avenue, Hampstead, N.W.3. HAREFIELD AND NORTHWOOD GROUP HOSPITAL MANAGEMENT COMMITTEE. RESIDENT MEDICAL OFFICER (House Officer grade) required.

Applications, with copies of testimonials, to the Administrative Officer.

LONDON HOSPITAL, Whitechapel, E.1. Applications are invited for the post of REGISTRAR in General Surgery becoming vacant in September, 1958. A higher qualification, although desirable, is not essential. The appointment will be for 1 year, renewable for a further year, 1 of which will be spent in the Department of Thoracic Surgery, or at the Hospital's Annexe at Brentwood:

Applications (10 copies), giving the names and addresses of 3 referees, should be received by the undersigned by 28th August, 1958. H. BRIERLEY, House Governor.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. 2 vacancies (1 resident, 1 non-resident) occur 1st October, 1958, for HOUSE PHYSICIANS. Appointments for 6 months, 4 in London, 2 at the Country Branch, near Letchworth, and post graded as House Officer. Duties include work in the Outpatient Department and Special Clinics as well as in wards. The resident post will be attached to the Cardiological firm during the 4 months in London.

Applications, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should reach the undersigned not later than 20th August.

J. ROBBINS, House Governor.

London Chest Hospital, E.2.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. A vacancy occurs 1st October, 1958, for RESIDENT SURGICAL OFFICER. Appointment for 6 months, with prospect of renewal. Post graded as Senior House Officer or Registrar, according to qualifications and previous surgical experience.

Applications, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 recent testimonials, should reach the undersigned not later than 20th August. J. ROBBINS, House Governor.

London Chest Hospital, E.2.

METROPOLITAN HOSPITAL, Kingsland-road, London, E.8. (General, 146 Beds.) Applications are invited for the pre-registration post of HOUSE SURGEON, now vacant.

Applications from provisionally and fully registered candidates, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to the Hospital Secretary, as soon as possible.

MOORFIELDS EYE HOSPITAL (City-road Branch), London, E.C.1. Applications are invited for the post of SIXTH HOUSE SURGEON (Registrar), non-resident. The appointment is for a period of 4 months from 1st November, 1958, and the holder of the post at the completion of that time will be eligible for appointment as Fifth, Fourth, Third, Second Resident Surgical Officer, and subsequently as Senior Resident officer, for similar periods.

Applications should be submitted on the official form obtainable from the undersigned, stating age and qualifications, together with testimonials and photograph, and be received not later than 22nd August, 1958.

J. P. HEMING, House Governor.

PLAISTOW HOSPITAL, Samson-street, E.13. (211 Beds.) Applications are invited for the appointment of RESIDENT HOUSE OFFICER (post-registration or pre-registration second post) for 6 months commencing 1st October, 1958, in the Chest Unit and Infectious Diseases Unit (if possible, appointment to be preceded by 2 weeks' Locum); some experience in diseases of the chest desirable. The position offers good opportunity for experience in general medicine.

Applications, with copies recent testimonials, to Hospital Secretary by 13th August, 1958.

PUTNEY HOSPITAL, Lower Common, London, S.W.15. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SURGICAL REGISTRAR (resident), F.R.C.S. For 1 year in the first instance from October, 1958. Holder required as part of his duties to act as Group Admissions Officer, alternate periods of 3 months.

Forms of application, obtainable from the Group Secretary, Battersea and Putney Group Hospital Management Committee, St. John's Hospital, S.W.11, to be returned completed within 14 days.

NATIONAL HOSPITALS FOR NERVOUS DISEASES. Applications are invited from registered medical practitioners for the appointment of NON-RESIDENT HOUSE PHYSICIAN at The National Hospital, Queen-square, W.C.1, to commence 1st November, 1958. There are 2 vacancies. These posts carry the grade of Senior House Officer. The appointments will be for 6 months.

Applications, with names of 3 referees, to be sent to the undersigned not later than 22nd August, 1958.

H. EWART MITCHELL, Secretary to the Board of Governors.
The National Hospitals for Nervous Diseases,
Queen-square, London, W.C.1.

NEW END HOSPITAL, London, N.W.3. Applications are invited for the post of HOUSE PHYSICIAN (general medicine) vacant 1st October, 1958. Preference will be given to pre-registration candidate.

Application forms from Group Secretary, 46, Cholmeley Park, N.6 (ARC. 3070, ext. 527), and returnable to the Surgeon-Superintendent, New End Hospital, by 19th August, 1958.

NEW END HOSPITAL, London, N.W.3. Applications are invited for 2 posts of HOUSE SURGEON (general surgery) vacant 1st October, 1958. Preference will be given to pre-registration candidates for 1 position.

Application forms from Group Secretary, 46, Cholmeley Park, N.6 (ARC. 3070, ext. 527), and returnable to the Surgeon-Superintendent, New End Hospital, by 19th August, 1958.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

Wanstead Hospital, Hermon Hill, E.11. REGISTRAR in Obstetrics and Gynæcology. Resident. Previous experience essential. Preference will be given to candidates who have obtained or are studying for M.R.C.O.G.

Hackney Hospital, E.9. REGISTRAR in Obstetrics and Gynæcology. Resident. Recognised for Gynæcology M.R.C.O.G.

Hackney Hospital, E.9. ANÆSTHETIC REGISTRAR, Resident or non-resident. Recognised for F.F.A. R.C.S. and D.A.

North Middlesex Hospital, Edmonton, and annexes. ANÆSTHETIC REGISTRAR. Non-resident. Offers wide experience in anæsthetics. Recognised for F.F.A. R.C.S. and D.A.

Claybury Hospital, Woodford Bridge, Essex (2200 Beds, 1400 admissions annually). PSYCHIATRIC REGISTRAR. All modern forms of treatment. Clinical conferences held weekly. Outpatient clinics at general hospitals. Facilities to attend D.P.M. classes in London. Recognised for D.P.M.

Appointments subject to review after 1 year.

Application forms from Secretary, 11A, Portland-place, W.1, to be returned by 23rd August.

NORTH MIDDLESEX HOSPITAL, London, N.18. Senior HOUSE OFFICER (pædiatrics), resident, required for 1st October (Locum 13th–30th September). Appointment for 6 months in the first instance, with possible extension to 1 year. Previous experience desirable. Recognised for D.C.H.

Applications, giving full particulars, with copies of recent testimonials and/or names of 2 referees, to Secretary of Hospital, by 13th August.

NORTH MIDDLESEX HOSPITAL, London, N.18. Locum SENIOR REGISTRAR in Anæsthetics required from 1st September for 6 weeks. Full-time, if possible. Non-resident, but on call on certain nights for serious emergencies.

Applications, stating age, qualifications, experience, with copies of recent testimonials, and names of 2 referees, to Secretary of Hospital.

QUEEN ELIZABETH HOSPITAL FOR CHILDREN, Hackney-road, E.2; Shadwell, E.1; and BANSTEAD, SURREY. HOUSE OFFICER appointment for 2 consecutive periods of 6 months, commencing 1st October, 1958; first period House Physician, Hackney-road (6 months); second period House Surgeon, Hackney-road (2 months) and Casualty Officer, Shadwell (4 months).

Application forms may be obtained from the Secretary at Hackney-road, and should be returned, with not more than 3 testimonials, not later than 16th August, 1958.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, E.15. SENIOR CASUALTY OFFICER (Male or Female, Senior House Officer grade) for 1 year commencing 19th September, 1958. Post recognised for F.R.C.S. (i.e., half the year is recognised as casualty and half as general surgery).

Applications, with names of 2 referees, to Hospital Secretary by 15th August, 1958.

ROYAL FREE HOSPITAL, Gray's Inn-road, W.C.1. Applications are invited from registered medical practitioners for the post of SENIOR CASUALTY OFFICER. The appointment is full-time, resident, for 6 months, duties to commence on 1st October, 1958. Salary and conditions of service in accordance with those laid down by the Ministry of Health for Senior House Officers.

Application forms may be obtained from the Secretary to the Board of Governors, to whom they should be returned not later than 15th August, 1958.

ROYAL FREE HOSPITAL, Gray's Inn-road, W.C.1. Applications are invited for the post of SENIOR RESIDENT ANÆSTHETIST. The appointment is for 6 months, duties to commence 1st October, 1958. Salary in accordance with the Ministry of Health scale for House Officers.

Application forms may be obtained from the Secretary to the Board of Governors, to whom they should be returned not later than 20th August, 1958.

ROYAL FREE HOSPITAL, Gray's Inn-road, W.C.1. Applications are invited for the post of JUNIOR RESIDENT ANÆSTHETIST. The appointment is for 6 months, duties to commence 1st October, 1958. Salary in accordance with the Ministry of Health scale for House Officers.

Application forms may be obtained from the Secretary to the Board of Governors, to whom they should be returned not later than 20th August, 1958.

ROYAL MARSDEN HOSPITAL, Fulham-road, S.W.3. Applications are invited for the post of SURGICAL SENIOR REGISTRAR. Appointment will be for 3 or 4 sessions as arranged from October, 1958. Post is open only to candidates who hold Consultant or Senior Hospital Medical Officer sessions elsewhere, or have completed a period of training as Senior Registrars or are from overseas and wish to take a period of advanced training for not more than 2 years. Candidates must hold F.R.C.S. diploma.

Applications on a form obtainable from the House Governor to be submitted by 29th August.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, S.W.4. Applications are invited from pre-registration and registered Female practitioners for the appointment of HOUSE SURGEON. Vacant 24th October, 1958, for a period of 6 months. Recognised for the F.R.C.S.

Forms of application from the Hospital Secretary.

SOUTH LONDON HOSPITAL FOR WOMEN, Clapham Common, S.W.4. Applications are invited from pre-registration and registered Female medical practitioners for the appointment of OBSTETRIC HOUSE SURGEON. Recognised for the M.R.C.O.G. Appointment for 6 months from 24th October, 1958.

Forms of application from Hospital Secretary.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, S.W.4. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited from registered Women medical practitioners for the post of Full-time SURGICAL REGISTRAR (recognised for the F.R.C.S.). Resident or non-resident if living near Hospital. Vacant now. The appointment is normally for 2 years, but subject to review at end of first year. Canvassing will disqualify, but candidates are invited to visit the Hospital if they so desire.

Forms of application from the Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11, to whom completed applications should be returned not later than 23rd August, 1958.

SPRINGFIELD HOSPITAL, Tooting, S.W.17. Locum PSYCHIATRIC REGISTRAR required immediately for approximately 2 months.

Applications, stating age, qualifications and experience, together with names of 3 referees, to be sent to Physician-Superintendent.

ST. ANDREW'S HOSPITAL, Bow, E.3. Locum Tenens ANÆSTHETIC REGISTRAR required at above Hospital from 11th August, 1958, for approximately 2 months.

Please apply immediately to Hospital Secretary—telephone EAST 2030.

ST. GEORGE'S HOSPITAL, S.W.1. Applications are invited for the post of REGISTRAR to the Radiotherapy Department. Candidates should possess the Diploma in Medical Radiotherapy or similar qualifications. The appointment is for 1 year in the first instance, and the successful candidate will be required to take up his duties as soon as possible.

Applications, giving details of age, education, qualifications, experience, and the names of 2 referees, should reach the undersigned not later than 6th September, 1958.

P. H. CONSTABLE, House Governor.

ST. BARTHOLOMEW'S HOSPITAL, London, E.C.1. Applications are invited for the post of REGISTRAR in the Radiotherapy Department. The post is tenable from 1st October next or by arrangement, and is for 1 year in the first instance, with possible re-election for a second year.

Applications, with the names of 2 referees, should be submitted to the undersigned within the next 21 days.

C. C. CARUS-WILSON, Clerk to the Governors.

ST. JAMES' HOSPITAL, Balham, London, S.W.12. SENIOR HOUSE OFFICER (gynæcology). Post vacant 16th August. Recognised for M.R.C.O.G.

Applications, stating age, qualifications, experience and names of 2 referees, to Group Secretary, Wandsworth Hospital Group, at above address.

ST. JAMES' HOSPITAL, Balham, London, S.W.12. SENIOR HOUSE OFFICER (orthopædic and trauma). Post vacant 25th August. Recognised for F.R.C.S.

Applications, stating age, qualifications, experience and names of 2 referees, to Group Secretary, Wandsworth Hospital Group, at above address by 16th August.

ST. JAMES' HOSPITAL, Balham, London, S.W.12. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SURGICAL REGISTRAR required. Post vacant 1st October. Applicants should possess F.R.C.S.

Application forms, obtainable from Group Secretary, Wandsworth Hospital Group, at above address, to be completed and returned by 23rd August.

ST. LEONARD'S HOSPITAL, Nuttall-street, London, N.1. (General—192 Beds.) Applications are invited from registered or provisionally registered medical practitioners for the post of HOUSE PHYSICIAN for 6 months.

Applications, with 2 recent testimonials, to be sent to the Hospital Secretary by 16th August, 1958. Applications may be sent in pending the qualifying examination results being known, and provided these are available at the date of interview.

ST. MARY'S HOSPITAL, W.2. Part-time Registrar to the Psychiatric Department (5 sessions per week) for first period of 12 months from 1st October, 1958. Previous experience in psychiatry necessary and preference given to candidates holding the D.P.M.

Full details, with names and addresses of 3 referees, must reach the House Governor by 26th August, 1958.

ST. NICHOLAS HOSPITAL, Plumstead, S.E.18. Senior HOUSE OFFICER (Casualty, Orthopædic, and Fracture Departments). Recognised for F.R.C.S. 6-month resident appointment and may then be renewed. Salary £819 10s. p.a., less £150 p.a. for residence.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ST. THOMAS'S HOSPITAL and the SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. (Joint appointment.) Whole-time SENIOR REGISTRAR to the Children's Department at St. Thomas's and Lambeth Hospitals, for 1 year in the first instance from 1st October, 1958. 8 sessions per week at St. Thomas's Hospital and 3 sessions per week at the Lambeth Hospital.

Applications (9 copies), naming 3 referees, to the Clerk of the Governors, St. Thomas's Hospital, S.E.1, by 19th August, 1958.

ST. THOMAS'S HOSPITAL and the SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. (Joint appointment.) Whole-time SENIOR SURGICAL REGISTRAR at St. Thomas's Hospital and the 3 major Portsmouth hospitals to work mainly at St. Thomas's Hospital, and, subject to annual reappointment, may be required to spend 1 year at Portsmouth.

Applications (9 copies), with names of 2 referees, to the Clerk of the Governors, St. Thomas's Hospital, S.E.1, by 23rd August, 1958.

ST. THOMAS'S HOSPITAL, London, S.E.1. Senior REGISTRAR to the Department of Anæsthetics for a period of 1 year in the first instance. Whole-time.

Applications (5 copies), naming 2 referees, to the Clerk of the Governors by 5th September, 1958.

ST. THOMAS'S HOSPITAL, London, S.E.1. Registrar to the Cardiac Department for a period of 1 year in the first instance.

Applications, naming 2 referees, to the Clerk of the Governors by 20th August, 1958.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in General Surgery to fill a vacancy in the approved trainee establishment in the Camberwell Group of hospitals, as from 22nd October, 1958. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 23rd August, 1958.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment vacant from 1st October, 1958, as Whole-time REGISTRAR in General Medicine at Dulwich Hospital, East Dulwich-grove, S.E.22, in the Camberwell Group of hospitals, where there is an association with King's College Hospital Medical School for teaching purposes. The appointment may be resident or non-resident, but if non-resident the successful candidate will be required to sleep in during nights when on duty. No married quarters are available. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 23rd August, 1958.

TAVISTOCK CLINIC, 2-4, Beaumont-street, London, W.1. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the Whole-time post of SENIOR REGISTRAR in Psychiatry (Adult Department). Post vacant 1st October, 1958. Appointment for 1 year in the first instance. Applicants must have good general experience in psychiatry, and preference will be given to candidates possessing D.P.M., and who have had or are having personal analytic training. Clinic may be visited by direct appointment.

Application forms obtainable from and returnable to Secretary, Paddington Group Hospital Management Committee, Harrow-road, W.9, by 25th August, 1958.

UNIVERSITY COLLEGE HOSPITAL and the NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for a joint SENIOR REGISTRARSHIP in the X-ray Diagnostic Departments of University College Hospital (7 half-days a week) and of the Whittington Hospital, N.19 (4 half-days a week) for 1 year in the first instance from 29th September, 1958.

Applications, with names of 2 referees, to T. F. W. MACKEOWN, Administrator and Secretary, University College Hospital, Gower-street, W.C.1, by 23rd August, 1958.

WANSTEAD HOSPITAL, Hermon Hill, E.11. (191 Beds.) Applications are invited for the post of CASUALTY OFFICER (recognised for F.R.C.S.). Graded Senior House Officer. Vacant 14th August, 1958. Salary £819 10s. p.a., less £150 p.a. for board, lodging, &c.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

WANSTEAD HOSPITAL, Hermon Hill, London, E.11. (191 Beds.) HOUSE SURGEON required. Recognised for F.R.C.S.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

WEST LONDON HOSPITAL, Hammersmith-road, London, W.6. Locum Tenens Whole-time NON-RESIDENT SURGICAL REGISTRAR required for 8 weeks commencing 1st September.

Applications, stating age, qualifications and experience, with copies 2 recent testimonials, to Secretary by 26th August.

WEST LONDON HOSPITAL, Hammersmith-road, London, W.6. RESIDENT HOUSE OFFICER (pædiatrics, E.N.T., ophthalmic, dental and dermatology) required 17th September.

Detailed applications, copies 2 recent testimonials, to Secretary, by 25th August.

WEST LONDON HOSPITAL, Hammersmith-road, London, W.6. RESIDENT CASUALTY OFFICER (Senior House Officer grading) required for 6 months from 8th September.

Detailed applications, copies 2 recent testimonials, to Secretary immediately.

WEST LONDON HOSPITAL, Hammersmith-road, London, W.6. RESIDENT HOUSE SURGEON (general and gynæcology) required 27th August. Pre-registration post.

Detailed applications, copies 2 recent testimonials, to Secretary, immediately.

WHIPPS CROSS HOSPITAL, London, E.11. Leytonstone (NO. 10) HOSPITAL GROUP. Applications are invited for the post of SENIOR HOUSE OFFICER (Casualty Officer) at above Hospital. This post, which is recognised by the Royal College of Surgeons for 6 months' casualty training under the Fellowship regulations, is vacant now.

Application forms are obtainable from the Hospital Secretary, to whom they should be returned by 19th August, 1958.

ABERYSTWYTH, CARDIGANSHIRE. GENERAL HOSPITAL. MID-WALES HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (surgical) required (resident). Post recognised for F.R.C.S. examination. Vacancy immediate.

Applications, stating age, experience, &c., to the Group Secretary, Mid-Wales Hospital Management Committee, 31, North-parade, Aberystwyth, Cardiganshire.

ASHFORD HOSPITAL, Ashford, Middlesex. (560 Beds.) STAINES GROUP HOSPITAL MANAGEMENT COMMITTEE. Required, RESIDENT HOUSE PHYSICIAN for general medical duties. 6-month appointment, vacant 8th September, 1958. Preference given to pre-registration candidates.

Applications, stating age, qualifications and experience, with copies of up to 3 recent testimonials, to Medical Director of Hospital.

ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (obstetrics/gynæcology) required at Ashton-under-Lyne General Hospital. Bed complement 75 obstetric and 26 gynæcology. Recognised for M.R.C.O.G.

Applications, with copies of 2 testimonials, to Group Secretary, General Hospital, Ashton-under-Lyne, Lancs.

AYLESBURY. ROYAL BUCKINGHAMSHIRE HOSPITAL. CASUALTY OFFICER (Senior House Officer) required mid-August. Post recognised for F.R.C.S. Self-contained furnished flat available at moderate rental.

Apply, with copies of 2 recent testimonials, to Secretary-Superintendent.

BARNSTAPLE. NORTH DEVON INFIRMARY. (105 Beds.) HOUSE SURGEON (pre-registration); vacant now. The Hospital serves a wide area of pleasant countryside, and the post affords good opportunity to study excellent clinical material.

Apply to Group Secretary, 19, Alexandra-road, Barnstaple, N. Devon.

BARNSTAPLE. NORTH DEVON INFIRMARY. (Central Group Hospital of 105 Beds.) SENIOR HOUSE SURGEON post vacant immediately for 1 year. Salary £819 10s. p.a. 5-roomed furnished flat available for rental.

Applications, with customary details, to Group Secretary, North Devon Hospital Management Committee, 19, Alexandra-road, Barnstaple.

BARNSTAPLE. NORTH DEVON INFIRMARY. (105 Beds.) HOUSE PHYSICIAN (pre-registration) required from 5th September, 1958.

Applications, naming 2 referees, to Group Secretary, North Devon Hospital Management Committee, 19, Alexandra-road, Barnstaple.

BATLEY. THE GENERAL HOSPITAL. (99 Beds.) SENIOR HOUSE SURGEON (orthopædics and general surgery). This Hospital is the main orthopædic hospital in the Group and has 36 orthopædic and 14 general surgery beds. The appointment falls vacant on 10th August, 1958, and is normally held for 12 months. It is recognised by the Royal College of Surgeons of England for a period of 6 months' training for the final examination. If required, a desirable furnished house is available, on rental, close to the Hospital.

Applications, giving full details of present and past appointments and names and addresses of 3 referees, should be forwarded to the Administrative Officer at the General Hospital, Batley, not later than 23rd August, 1958.

BEDFORD GENERAL HOSPITAL. (431 Beds.) House SURGEON required. Pre- or post-registration; recognised for F.R.C.S. Vacant mid-August. Post offers exceptional opportunities for general experience in busy acute surgical units.

Inquiries and applications, with copies of 2 recent testimonials, to be sent immediately to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 acute beds.) ORTHOPÆDIC HOUSE SURGEON with some general surgery (House Officer or Senior House Officer grading according to experience). Vacant now. Approved pre-registration post. Fully registered practitioners may apply. Recognised for F.R.C.S. Married quarters may be available.

Apply Group Secretary.

BIRMINGHAM (near). MARSTON GREEN MATERNITY HOSPITAL, Berwicks-lane, MARSTON GREEN, near BIRMINGHAM. SENIOR HOUSE OFFICER in Pædiatrics (resident) required 1st October, 1958, for 6 months or 1 year (the latter recognised for D.C.H.). Duties in Premature Baby Unit (12 cots); in Neonatal Department at above Hospital (121 Beds) (Hospital affiliated to University of Birmingham for teaching of students); and in Neonatal and Children's Departments at neighbouring hospitals. Previous pædiatric or obstetric experience desirable.

Detailed applications, together with copies of 2 recent testimonials, to the Group Secretary, Dudley Road Hospital, Birmingham, 18, by 15th August, 1958.

BIRMINGHAM, 29. SELLY OAK HOSPITAL. (Equipped beds—1033.) HOUSE SURGEON (pre-registration), now vacant. Recognised for F.R.C.S.

Apply immediately to the Medical Superintendent, giving qualifications, age, experience and enclosing copies of 3 testimonials.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE BIRMINGHAM MATERNITY HOSPITAL. Applications are invited from registered medical practitioners for the post of RESIDENT OBSTETRIC HOUSE SURGEON vacant 1st November, 1958. The appointment is recognised for the M.R.C.O.G. and D.Obst.R.C.O.G.

Application forms obtainable from the House Governor, the Birmingham and Midland Hospitals for Women, Showell Green-lane, Sparkhill, Birmingham, 11, to be returned not later than 30th August, 1958. G. A. PHALP, Secretary.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the post of RESIDENT REGISTRAR in Anæsthetics to the United Birmingham Hospitals. The appointment is tenable for 1 year in the first instance. Preference will be given to candidates who have passed Part I, D.A., or Primary F.F.A. R.C.S.

Application forms may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, and should be returned to him as soon as possible.

BISHOP AUCKLAND. THE GENERAL HOSPITAL. (350 Beds.) HOUSE SURGEON required. Recognised pre-registration appointment. Accommodation available for married officer with no children.

Apply, naming 2 referees, to Group Secretary, South West Durham Hospital Management Committee, by 16th August.

BISHOP'S STORTFORD, HERTFORDSHIRE. HERTS AND ESSEX GENERAL HOSPITAL. Applications invited for post of HOUSE OFFICER (surgical—pre-registration). Salary £467 10s. –£522 10s. p.a. less £125 for residential emoluments. Appointment to commence immediately.

Applications, stating age, nationality, qualifications and experience, with copies of 2 testimonials or names of referees, to Hospital Secretary.

BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.

Royal Infirmary, Blackburn

HOUSE SURGEON required immediately. Post recognised for F.R.C.S. and approved for pre-registration purposes.

Queen's Park Hospital, Blackburn

HOUSE SURGEON required immediately. Post recognised for F.R.C.S. and approved for pre-registration purposes.

Victoria Hospital, Accrington

HOUSE PHYSICIAN required immediately. Post recognised for pre-registration purposes.

Apply to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (anæsthetics) required immediately for duties throughout the Group, mainly at Royal Infirmary, Blackburn. Residence at Royal Infirmary, Blackburn. Post recognised for D.A. and F.F.A. R.C.S.

Applications to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn, giving names of 2 referees.

BOLTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.

Bolton District General Hospital (607 Beds)

RESIDENT SENIOR HOUSE OFFICER for general surgical duties. Vacant 28th August, tenable for 12 months and recognised for F.R.C.S.

RESIDENT HOUSE SURGEON. Now vacant, tenable for 6 months, and recognised under pre-registration service scheme; also recognised for F.R.C.S.

RESIDENT HOUSE PHYSICIAN. Now vacant, tenable for 6 months and recognised under pre-registration service scheme.

The Royal Infirmary, Bolton (238 Beds)

RESIDENT HOUSE SURGEONS (2). Now vacant, tenable for 6 months, and recognised under pre-registration service scheme. Also recognised for F.R.C.S.

Applications, stating age, nationality, qualifications, experience and the names of 2 referees, to Group Secretary, The Royal Infirmary, Bolton.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road, BOSCOMBE. (494 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of a RESIDENT or NON-RESIDENT SENIOR HOUSE OFFICER in Pathology. The successful applicant will have opportunities for gaining experience in all 4 departments of the Laboratory, which is recognised for the Diploma in Pathology.

Applications to the Hospital Secretary.

BRIGHTON AND LEWES HOSPITAL MANAGEMENT COMMITTEE GROUP HOSPITALS. (78 Beds.) SENIOR HOUSE OFFICER for duties in the E.N.T. Department of the above Group. Vacant beginning of August. Recognised for F.R.C.S. and D.L.O.

Applications, with details of experience, &c., together with names of 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRIGHTON GENERAL HOSPITAL. Applications are invited for the appointment of HOUSE SURGEON (orthopædics). Salary in accordance with national scale. This is a pre-registration appointment.

Applications, stating age, qualifications, and experience, and giving the names of 2 referees, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton.

BRIGHTON. NEW SUSSEX HOSPITAL FOR WOMEN AND SUSSEX MATERNITY HOSPITAL. BRIGHTON AND LEWES HOSPITAL MANAGEMENT COMMITTEE. GYNÆCOLOGICAL AND OBSTETRIC HOUSE SURGEON (Female) required 17th September, 1958. Gynæcological Department (24 Beds) at New Sussex Hospital and relief obstetrical work at Sussex Maternity Hospital (62 Beds). Post recognised for M.R.C.O.G.

Applications, giving age, experience, and 2 references, to be sent to the Administrative Officer, New Sussex Hospital, Windlesham-road, Brighton, by 21st August, 1958.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (314 Beds.) CASUALTY HOUSE SURGEON required end August. Duties include work in orthopædic and traumatic unit. Recognised for pre-registration and F.R.C.S.

Applications, stating age, qualifications, experience, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRIGHTON. SUSSEX EYE HOSPITAL. (56 Beds.) SENIOR HOUSE SURGEON (Senior House Officer grade) and HOUSE SURGEON required end of August. Both posts recognised for F.R.C.S. and D.O. Successful applicant for the post of House Surgeon will be considered for the senior post on completion of 6 months.

Applications, stating usual particulars, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BURNLEY GENERAL HOSPITAL. (641 Beds.) Resident HOUSE OFFICER (medical). The appointment is approved as a pre-registration post. Vacant 25th September, 1958.

Applications, with 2 references, to Group Secretary, Burnley and District Hospital Management Committee, Burnley General Hospital.

BURTON-ON-TRENT. THE GENERAL HOSPITAL. HOUSE OFFICER (orthopædics) (pre-registration post) required at the above Hospital. Recognised for F.R.C.S.

Applications to Group Secretary as soon as possible.

BURY AND ROCHDALE HOSPITAL GROUPS. Resident REGISTRAR in Psychiatry. Post now vacant.

Apply to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, Lancs.

BRISTOL (near). HAM GREEN HOSPITAL, Pill, near BRISTOL. Applications are invited for the post of RESIDENT JUNIOR HOSPITAL MEDICAL OFFICER in the Chest Diseases Wards of the above Hospital. The Hospital is fully equipped for modern treatment of pulmonary tuberculosis and other diseases of the chest, including regular major thoracic surgery. Opportunity also for work in the Bristol Chest Clinic. Appointment for 1 year—renewable. Post vacant 1st September, 1958.

Applications, with testimonials and names of referees, to the Secretary, Ham Green Hospital, Pill, near Bristol.

BRISTOL MENTAL HOSPITAL MANAGEMENT COM-MITTEE. BARROW AND FISHPONDS HOSPITALS. Applications invited from registered practitioners for appointment of SENIOR HOUSE OFFICER. National scale and conditions. The Group includes modern Admission Units, Neurosis Centre and Day Hospital, with departments of applied psychology and electroencephalography. The appointment offers opportunities for experience in many aspects of acute and chronic psychiatric illness. Facilities available for studying and gaining experience for Diploma in Psychological Medicine and for attending courses at Bristol University in preparation for this examination. Full board-residence available for single officer.

Applications, with names of 3 referees, should be sent to Medical Superintendent, Barrow Hospital, Barrow Gurney, near Bristol.

BRISTOL. COSSHAM AND FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. FRENCHAY HOSPITAL. (496 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (Medical). The appointment, which will be for 1 year in the first instance, is on the terms and conditions of service for hospital medical staff and is at a salary of £819 10s., less a deduction of £150 p.a. in respect of unmarried accommodation provided at the Hospital. The candidate appointed will have general supervision under the Consultant Staff of the 89 Beds for general medicine and will be attached as a Clinical Assistant for occasional duties which may be required in the Regional Departments of Neurosurgery, Thoracic Surgery and Plastic Surgery at the Hospital. As the Senior Resident Medical Officer he will be in charge of the "House" and his duties will include pre-employment medical examinations of staff appointed by the Management Committee. It is customary for the resident nursing staff to be invited to register on the patients' panel of the Senior Resident Medical Officer, who is entitled to retain the appropriate fees receivable.

Applications, containing details of qualifications and experience, together with the names of 2 referees, should be forwarded to the Group Secretary, Frenchay Hospital, Bristol, not later than 14th August, 1958.

CAMBRIDGE. ADDENBROOKE'S HOSPITAL. Medical REGISTRAR (non-resident) for 1 year in the first instance from mid-October, renewable for second year.

Apply, with full particulars and names of 3 referees, to Secretary by 23rd August, 1958.

CAMBRIDGE. THE UNITED CAMBRIDGE HOS-PITALS. ADDENBROOKE'S HOSPITAL, CAMBRIDGE. HOUSE SURGEON for 6 months from 28th September. Recognised pre-registration service.

Apply to the Secretary by 23rd August, stating age, nationality, qualifications, and experience with dates, and with copies of 3 testimonials. Interviews early September.

CAMBRIDGE. THE UNITED CAMBRIDGE HOS-PITALS. ADDENBROOKE'S HOSPITAL, CAMBRIDGE. HOUSE PHYSICIAN for 6 months from 4th October. Recognised pre-registration service.

Apply to the Secretary by 23rd August, stating age, nationality, qualifications, and experience with dates, and with copies of 3 testimonials. Interviews early September.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) The post of PÆDIATRIC HOUSE PHYSICIAN, recognised for D.C.H., includes work in the ward and Outpatient Department and also provides experience in the care of the newborn. Opportunities exist for the study of preventive medicine among children and child guidance work. Post vacant end of September, 1958. National Health Service salary and conditions.

Applications, together with copies of 2 testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CANTERBURY. KENT AND CANTERBURY HOS-PITAL. (277 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (casualty) which becomes vacant mid-September, 1958. Salary £819 10s. p.a. Recognised for the F.R.C.S.

Applications to be sent to the Hospital Secretary at the above Hospital, together with copies of 3 recent testimonials.

CANTERBURY. KENT AND CANTERBURY HOS-PITAL. (277 Beds.) GYNÆCOLOGICAL HOUSE SURGEON required at Highland Court Annexe, a unit of 25 gynæcological beds situated 3 miles from the above Hospital, with all ancillary services available. Recognised for M.R.C.O.G. 6 months' appointment. Post vacant mid-September. National Health Service salary and conditions.

Applications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CARDIFF. THE UNITED CARDIFF HOSPITALS. Applications are invited for the appointment of SENIOR HOUSE OFFICER in Anæsthetics. Non-resident post, commencing 1st October, 1958. Appointment based at the Cardiff Royal Infirmary, but will include duties at other hospitals in the area.

Application forms are available from the Secretary to the Board at the Cardiff Royal Infirmary, Newport-road, Cardiff, and should be returned within 14 days of the appearance of this advertisement.

CARDIFF. THE UNITED CARDIFF HOSPITALS. Applications are invited for the post of REGISTRAR in Anæsthetics, to commence duty 1st October. The successful candidate will work as a member of the Department of Anæsthetics, partly in the Teaching Hospitals and partly in other hospitals in the area. Duties may include undergraduate teaching and assisting with research.

Application forms are available from the Secretary to the Board at the Cardiff Royal Infirmary, Newport-road, Cardiff, and should be returned within 14 days of the appearance of this advertisement.

CARDIFF. THE UNITED CARDIFF HOSPITALS. Applications are invited for the post of SENIOR HOUSE OFFICER in Pædiatrics at Llandough Hospital, Penarth. The post is a resident one, commencing 1st October, and provides excellent experience for those entering general practice. Pædiatric experience desirable but not essential.

Application forms are available from the Secretary to the Board at the Cardiff Royal Infirmary, Cardiff, and should be returned within 14 days of the appearance of this advertisement.

CHESTER-LE-STREET. GENERAL HOSPITAL. (204 Beds.) SENIOR HOUSE OFFICER (general medicine). Post now vacant.

Apply, with names and addresses of 2 referees, to Group Secretary, Dryburn Hospital, Durham.

CHESTER-LE-STREET. GENERAL HOSPITAL. (204 Beds.) HOUSE PHYSICIAN (general medicine). Approved pre-registration post. Post now vacant.

Apply, with names and addresses of 2 referees, to Group Secretary, Dryburn Hospital, Durham.

CARSHALTON, SURREY. ST. HELIER HOSPITAL. (733 Beds.) CASUALTY OFFICERS (2), Senior House Officers. Posts recognised for F.R.C.S. Vacant 10th and 17th September, respectively.

Applications, stating age, qualifications, and experience, with copies of testimonials and the names of 2 referees, should be sent to the Group Secretary at above address.

CHELMSFORD, ESSEX. BROOMFIELD HOSPITAL. Required, experienced Locum Tenens SENIOR REGISTRAR for 6 months from 1st September, 1958, full residence or only when on duty. Unit has 312 Beds for the treatment of pulmonary tuberculosis in adults. Tuberculous and non-tuberculous thoracic surgery, chest clinics, and mass radiography.

Apply Physician-Superintendent.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL. WOKING AND CHERTSEY GROUP. (430 Beds.) ROYAL SURREY COUNTY HOSPITAL. GUILDFORD GROUP. (233 Beds.) Locum Full-time E.N.T. REGISTRAR for above and other hospitals in the Groups concerned required from 30th August, 1958, to 14th December, 1958. Recognised for F.R.C.S. and D.L.O. The hospitals may be visited by arrangement.

Applications to Physician-Superintendent, St. Peter's Hospital. Telephone: St. Peter's Hospital, Ottershaw 441; Royal Surrey County Hospital, Guildford 2323.

CHICHESTER. ST. RICHARD'S HOSPITAL. (400 Beds.) CHICHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Required, HOUSE SURGEON (pre-registration) for 6 months only in the first instance. Post vacant now. The Man or Woman appointed will work primarily in the surgical wards of the Hospital. Hospital recognised for F.R.C.S.

Applications, stating age, qualifications and experience, giving names of 2 persons from whom reference may be obtained, should be sent to the Surgeon-Superintendent.

COLCHESTER. ESSEX COUNTY HOSPITAL. (189 Beds.) Applications invited for post of SENIOR HOUSE OFFICER to Casualty and Radiotherapy Departments. Post tenable for 6 months or 1 year. Recognised for F.R.C.S.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for:—

Black Notley Hospital, Braintree, Essex (522 Beds)

Post of Locum SURGICAL REGISTRAR, for period 11th–24th August, 1958.

Post of Locum REGISTRAR for Pulmonary Tuberculosis Unit, including non-tuberculous diseases of the chest; also duties at chest clinics. Required 1st September for few months.

Locum Tenens ORTHOPÆDIC REGISTRAR with duties at Black Notley and Essex County Hospitals required immediately until mid-September; also some duties at the London Hospital.

Essex County Hospital, Colchester, Essex (181 Beds)

Post of Locum MEDICAL REGISTRAR required from 21st August, 1958.

Clacton and District Hospital, Clacton-on-Sea, Essex (58 Beds)

Post of TEMPORARY REGISTRAR required as Resident Casualty Officer for 2–3 months from 15th August, 1958.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

CREWE AND DISTRICT MEMORIAL HOSPITAL. (108 Beds—acute, and continuation 32 Beds.) SENIOR HOUSE OFFICER (casualty) required. Approved for F.R.C.S. Now vacant. Modern well-equipped department.

Apply immediately, stating age, qualifications, &c., with names of 2 referees, to reach the Group Secretary, South Cheshire Hospital Management Committee, Barony Hospital, Nantwich, Cheshire, within 7 days.

CROMER AND DISTRICT HOSPITAL, Cromer, Norfolk. CROMER AREA HOSPITAL MANAGEMENT COMMITTEE. Locum SENIOR HOUSE OFFICER required 1st to 14th September, 1958. Busy general hospital, 52 Beds with full range of specialties. Good holiday post. Pleasant seaside town. Locum rates £15 19s. per week.

Applications to Secretary, Cromer and District Hospital.

CROYDON. MAYDAY HOSPITAL. (595 Beds.) Croydon GROUP HOSPITAL MANAGEMENT COMMITTEE. ORTHOPÆDIC HOUSE OFFICER (Senior House Officer grade) required for 6 months in first instance. Post vacant 18th August, 1958.

Application forms obtainable from GEORGE A. PAINES, Group Secretary, Hospital Management Committee, General Hospital, London-road, Croydon.

CUCKFIELD HOSPITAL, Cuckfield, near Haywards HEATH. MID-SUSSEX HOSPITAL MANAGEMENT COMMITTEE. Vacancies as follows:—

JUNIOR HOUSE SURGEON (general surgery). Pre-registration post now vacant.

RESIDENT SENIOR HOUSE PHYSICIAN. Post vacant September.

Apply to Hospital Secretary, stating age, qualifications, nationality and experience, with names of 2 referees.

DARLINGTON MEMORIAL HOSPITAL. (314 Beds.) Applications are invited from Male or Female practitioners for the post of SENIOR HOUSE OFFICER (surgery), vacant 10th August, 1958. The post is recognised for the F.R.C.S. (Eng.). Salary £819 10s. p.a.; deduction of £150 for full residential emoluments. The post is tenable for 6 or 12 months.

Apply with references, stating age and experience, to G. W. BECKWITH, Group Secretary.

DRIFFIELD, YORKSHIRE. EAST RIDING GENERAL HOSPITAL. (247 Beds.) HOUSE SURGEON (first, second or third post). Vacant now. General surgery, casualty and some orthopædics. Approved pre-registration post. Fully registered practitioners may apply. Married quarters may be available.

Applications to Group Secretary, Westwood Hospital, Beverley, Yorkshire.

DERBY. DERBYSHIRE ROYAL INFIRMARY (416 Beds), DERBY CITY HOSPITAL (260 Beds). (Post recognised for training for D.A. and F.F.A. R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (anæsthetics) required for the above Hospitals. Duties also at other hospitals in the Group. This post offers special experience in neuro and orthopædic surgery and obstetrics. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 18th August, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

DONCASTER ROYAL INFIRMARY. (330 Beds.) Western HOSPITAL, DONCASTER. (241 Beds. Post recognised for M.R.C.O.G.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (obstetrics and gynæcology) required 25th September. Gynæcology beds at both hospitals; maternity unit at Western Hospital. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 18th August, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. SENIOR MEDICAL REGISTRAR, United Norwich Hospitals. Main hospital Norfolk and Norwich Hospital—441 Beds. By agreement with the Board of Governors of St. Bartholomew's Hospital, the fourth year in post may be spent on secondment to that hospital. Higher qualification necessary.

Applications, stating age, experience and the names of 3 referees, to the Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 1st September, 1958. Candidates invited to visit hospitals by direct arrangement with Hospital Management Committee Secretary, Norfolk and Norwich Hospital, Norwich.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. RESIDENT PÆDIATRIC HOUSE PHYSICIAN for above Hospital. Post vacant 24th September, 1958. 6 months' appointment. Post recognised for pre-registration purposes.

Applications, stating age, qualifications, experience and enclosing copies of up to 3 recent testimonials, to Medical Administrator of Hospital by 22nd August, 1958.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. (704 Beds.) RESIDENT HOUSE PHYSICIAN for Thoracic and Dermatological Departments. Duties to include "take in" of acute general medical cases. 6 months' appointment.

Applications, stating age, qualifications, experience and enclosing copies of up to 3 recent testimonials, to Medical Administrator of Hospital by 16th August, 1958.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. (704 Beds.) Locum CASUALTY REGISTRAR required at above Hospital from 25th August to 7th September inclusive.

Apply immediately to Medical Administrator, telephone EDGware 2381.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. Appointment of RESIDENT HOUSE SURGEON (third post). Vacant immediately. Post provides experience and duties in both general surgery and orthopædics. 6 months' appointment. Post recognised for F.R.C.S. by the Royal College of Surgeons.

Applications, with the names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, at Chase Farm Hospital.

ENFIELD. WAR MEMORIAL HOSPITAL, Chase Side, ENFIELD, MIDDLESEX. RESIDENT SENIOR HOUSE OFFICER required immediately for general medical and surgical duties in acute general hospital of 58 Beds. 12 months' appointment.

Applications, with names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, Chase Farm Hospital, The Ridgeway, Enfield, Middlesex.

EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom, SURREY. RESIDENT HOUSE SURGEON required immediately for Orthopædic, E.N.T., and Eye Departments. Post recognised for F.R.C.S.

Applications from fully or provisionally registered practitioners, stating age, qualifications, and experience, with copies of 2 recent testimonials, should be sent, as soon as possible, to Group Secretary, at above address.

EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom, SURREY. SENIOR HOUSE OFFICER (obstetrics and gynæcology) required 1st September. 12 months' appointment. Post recognised in obstetrics by the College for M.R.C.O.G. and D.Obst.R.C.O.G. purposes.

Applications, stating age, qualifications and experience, with copies of 2 recent testimonials, should be sent as soon as possible to Group Secretary at above address.

EXETER. WEST OF ENGLAND EYE INFIRMARY. (62 Beds.) EXETER AND MID-DEVON HOSPITALS MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER in Ophthalmology. Resident or non-resident. The post is recognised for the F.R.C.S. examination, and is vacant on 1st October, 1958.

Applications, with copies of 2 recent testimonials, to the Hospital Secretary by 23rd August, 1958.

GAINSBOROUGH. JOHN COUPLAND HOSPITAL. (40 Beds.) Locum RESIDENT MEDICAL OFFICER required. Junior Hospital Medical Officer grade. 18th August–17th September, 1958.

Apply in writing to Group Secretary, County Hospital, Lincoln.

GLASGOW. VICTORIA INFIRMARY. Applications are invited for the post of SENIOR HOUSE OFFICER in Orthopædics for duties at the Victoria Infirmary and a large unit at the Victoria Auxiliary Infirmary, Philipshill. The post is resident at Philipshill.

Applications, with names of 2 referees, should be sent forthwith to the Secretary, Board of Management for Glasgow Victoria Hospitals, 24, St. Vincent-place, Glasgow, C.1.

GLASGOW, E.3. ROBROYSTON HOSPITAL. Junior HOSPITAL MEDICAL OFFICER required. The work carried out consists mainly of tuberculous pulmonary disease, though substantial units exist for skeletal and urological tuberculosis. A small unit for acute respiratory diseases also exists, and there are units for non-tuberculous chest disease and for geriatrics. The post is non-resident and conditions of service and salary are in accordance with Whitley Council regulations.

Applications in writing should be made as soon as possible to the Physician-Superintendent.

GODALMING, SURREY. MILFORD CHEST HOSPITAL. (330 Beds.) THORACIC MEDICAL REGISTRAR required. The Hospital deals with all types of chest disease and has a large thoracic surgical centre for chest and heart disease. The person appointed will also be required to carry out duties at Guildford and Weybridge Chest Clinics. Accommodation available for a single person.

Application forms from the Group Secretary, Milford Chest Hospital, Godalming, Surrey, to whom they should be returned not later than 23rd August, 1958.

GODALMING, SURREY. MILFORD CHEST HOSPITAL. (330 Beds.) SENIOR HOUSE OFFICER required. The Hospital deals with all types of chest disease and has a large thoracic surgical centre for chest and heart disease. Accommodation available for a single person.

Apply, giving full details, with names of 3 referees, to the Physician-Superintendent by not later than 23rd August, 1958.

GRAVESEND AND NORTH KENT HOSPITAL, Gravesend, Kent. MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON. Applications are invited for this pre-registration post, vacant now. Post offers experience in obstetrics, gynæcology, and orthopædics as well as general surgery. Salary £467 10s.–£577 10s. p.a., according to experience.

Applications, stating age, qualifications, nationality and experience, to Hospital Secretary.

GREAT YARMOUTH AND GORLESTON GENERAL HOSPITAL, DENE SIDE, GREAT YARMOUTH. (134 Beds.) HOUSE SURGEON (House Officer or Senior House Officer status) required immediately. Post recognised for pre-registration service. Membership of a Medical Defence Society is a condition of appointment.

Applications, giving full details with names of 2 referees, to Hospital Secretary.

GRIMSBY GENERAL HOSPITAL. (Unit of 46 Beds.) GRIMSBY HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN (pre-registration) required for above Hospital. Medical library and reading facilities available.

Applications, with names of 2 referees, to the Hospital Secretary, Grimsby General Hospital, Grimsby.

GRIMSBY GENERAL HOSPITAL. Senior House Officer required for Casualty Department. Establishment consists of Senior Casualty Officer and 2 Senior House Officers. Excellent Medical Library taking principal periodicals.

Applications, with names of 2 referees, to Hospital Secretary.

HAILSHAM, SUSSEX. HELLINGLY HOSPITAL. Hailsham HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners (Male or Female) for the whole-time post of JUNIOR HOSPITAL MEDICAL OFFICER at the above Hospital. The post is a trainee appointment and offers experience in all branches of adult psychiatry. In addition, opportunities can be afforded for some experience in neurology and mental deficiency. The Hospital has a high admission-rate and is recognised for the D.P.M. Married or single accommodation is available.

Applications, giving the names of 3 referees, should be sent to the Medical Superintendent within 14 days of the appearance of this advertisement.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) HOUSE SURGEON. Pre-registration post for general surgery and urology required at this acute hospital (surgical) immediately.

Applications, with names of 2 referees, to Administrator.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) Applications are invited for the post of HOUSE SURGEON at the Royal East Sussex Hospital, Hastings. Pre-registration post recognised for F.R.C.S. Vacant 30th August, 1958. The Hospital is pleasantly situated facing the sea and is the main surgical hospital in the Hastings Group. Post offers excellent experience.

Applications, with names of 2 referees, to the Administrator.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) Applications are invited for the post of CASUALTY AND ORTHOPÆDIC HOUSE SURGEON (1 of 2 posts), graded Senior House Officer, for the Royal East Sussex Hospital, Hastings. Modern department. Hospital is pleasantly situated facing the sea. Post vacant now.

Applications, with names of 2 referees, to the Administrator.

HEREFORD. COUNTY HOSPITAL. Senior House OFFICER (pædiatrics) required, for unit of 60 Beds.

Applications in writing, together with names of 2 referees, to Group Secretary, Victoria House, Eign-street, Hereford.

HITCHIN, HERTFORDSHIRE. NORTH HERTS HOSPITAL. HOUSE SURGEON required. Post vacant end of August. Recognised as pre-registration post.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to the Medical Administrator, Lister Hospital, Hitchin, as soon as possible.

HILLINGDON HOSPITAL, Uxbridge, Middlesex. (621 Beds.) REGISTRAR for Otorhinolaryngology Department. Ample opportunity for practical operative experience. Post recognised for D.L.O. and for F.R.C.S. (England). Hospital may be visited by direct appointment.

Application forms obtainable from and returnable to Group Secretary, Uxbridge Group Hospital Management Committee, The Furze, Pield Heath-road, Uxbridge, Middlesex, by 19th August.

HILLINGDON HOSPITAL, Uxbridge, Middlesex. (General, 621 Beds.) PÆDIATRIC HOUSE PHYSICIAN. Duties include experience in general children's medical ward, neonatal unit, and pædiatric outpatient clinics. Post vacant mid-September. Appointment recognised for D.C.H. Applications accepted from registered or pre-registered practitioners.

Apply, stating age, qualifications, nationality and experience, with copies of not more than 3 recent testimonials, to Medical Director by 19th August.

HORNCHURCH. ST. GEORGE'S HOSPITAL. Junior HOSPITAL MEDICAL OFFICER (resident) required from approximately 1st September next at this Hospital which accommodates 404 chronic sick patients. The post offers excellent geriatric experience.

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford, as soon as possible.

HOVE GENERAL HOSPITAL. Pre-registration House PHYSICIAN required for a period of 6 months from 4th September, 1958. Excellent clinical material available and post is suitable for candidate working for a higher degree.

Applications, stating age, qualifications and full details of experience, together with names and addresses of 2 referees, to the Administrative Officer, Hove General Hospital, Sackville-road, Hove, 3.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from provisionally registered medical practitioners for the post of HOUSE PHYSICIAN to commence duties immediately. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Group Secretary,
Huddersfield Hospital Management Committee.
The Royal Infirmary, Huddersfield.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required to commence duty immediately. The post is recognised as a pre-registration appointment and for the F.R.C.S. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Secretary to the Management Committee.
The Royal Infirmary, Huddersfield.

HULL. KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT HOUSE SURGEON (recognised for the F.R.C.S. examinations). Pre-registration post.

Applications, with 2 recent testimonials, to the Hospital Secretary.

HULL. KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT HOUSE PHYSICIAN. Pre-registration post.

Applications, with 2 recent testimonials, to the Hospital Secretary.

HULL. VICTORIA HOSPITAL FOR SICK CHILDREN, Park-street. HOUSE SURGEON or Locum HOUSE SURGEON required immediately. An interesting and varied post and recognised for D.C.H.

Applications, together with details of experience, giving the names of 2 referees, should be sent to the Hospital Secretary.

HUNTINGDON COUNTY HOSPITAL. Applications are invited for the post of HOUSE OFFICER (medical), now vacant. The selected candidate will be required to look after medical and pædiatric cases and may be called upon to give emergency anæsthetics.

Apply, with full particulars and names of 2 referees, to Secretary, County Hospital, Huntingdon.

ILKLEY. MIDDLETON HOSPITAL. (386 Beds.) RESIDENT SENIOR HOUSE OFFICER (surgical) required for Major Thoracic Surgical Unit at the above Hospital. Eminently suitable for person intending to take Membership or Fellowship examination.

Applications, stating age, nationality, qualifications and experience, to Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL (Anglesea-ROAD WING). (350 Beds.) Applications invited for post of CASUALTY OFFICER (Senior House Officer grade) vacant 1st September, 1958. Post recognised for F.R.C.S. examinations.

Applications, stating age and nationality, together with copies of recent testimonials, to Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL (Heath-ROAD WING), IPSWICH. (280 Beds.) Applications invited for post of HOUSE PHYSICIAN (pre-registration), vacant 15th September, 1958.

Applications, giving details of qualifications, age, nationality, &c., together with copies of 3 recent testimonials, to Hospital Secretary.

IPSWICH. ST. HELEN'S HOSPITAL. (129 Beds for infectious diseases, pulmonary tuberculosis, long-stay orthopædics and geriatrics. The area Chest Clinic is in the Hospital.) HOUSE PHYSICIAN required (post-registration appointment). Accommodation available for married man.

Applications to JOHN WILLIAMS, Group Secretary, Ipswich Group Hospital Management Committee, at the Ipswich and East Suffolk Hospital (Anglesea-road Wing), Ipswich.

ISLEWORTH. SOUTH MIDDLESEX HOSPITAL. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR, whole-time, resident. Vacant now. Hospital admits all types of infectious diseases and offers wide clinical experience. Excellent opportunities for postgraduate studies. Candidates may visit Hospital by appointment with Physician-Superintendent.

Application forms obtainable from and returnable to Group Secretary, West Middlesex Hospital, Isleworth, by 19th August.

ISLEWORTH. SOUTH MIDDLESEX HOSPITAL. SENIOR HOUSE OFFICER for Ophthalmic Unit (29 Beds). Post recognised for F.R.C.S. and D.O. qualifications.

Applications, stating age, nationality, qualifications and experience, with copies of up to 3 recent testimonials, to Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 19th August.

KETTERING AND DISTRICT GENERAL HOSPITAL. CASUALTY OFFICER (Senior House Officer). Recognised for F.R.C.S. The post, vacant early September, 1958, offers wide experience of all traumatic conditions including fractures and some orthopædic cases, with charge of 30 Beds.

Applications, accompanied by testimonials, to be sent to the Group Secretary, General Hospital, Kettering.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-ON-THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of SENIOR HOUSE OFFICER (casualty and orthopædic) which is available on 1st October, 1958. The post is recognised in casualty for F.R.C.S. purposes.

Applications, stating age, qualifications, and experience, with 2 recent testimonials, should reach the Physician-Superintendent of the Hospital within 7 days of the appearance of this advertisement.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-ON-THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of SENIOR HOUSE OFFICER (pædiatrics) which is available on 1st October, 1958. The post is recognised for D.C.H. purposes.

Applications, stating age, qualifications and experience, with 2 recent testimonials, should reach the Physician-Superintendent of the Hospital within 7 days of the appearance of this advertisement.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-ON-THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of Locum REGISTRAR in Pædiatrics, which is available in early October, 1958.

Applications, stating age, qualifications and experience, together with 2 recent testimonials, should reach the Physician-Superintendent of the Hospital within 7 days of the appearance of this advertisement.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (197 Beds.) Locum HOUSE PHYSICIAN required, 12th–25th September inclusive.

Apply Hospital Secretary.

LEEDS REGIONAL HOSPITAL BOARD. Registrar vacancies.

General Surgery

(*a*) Huddersfield Group (100 general surgical beds). Residential accommodation available. Duties mainly at Huddersfield Royal Infirmary. Recognised for F.R.C.S. May include some duties in the Casualty Department

(*b*) Hull Royal Infirmary (80 general surgical beds) and other hospitals in the Hull A group.

Orthopædic Surgery

(*a*) Woodlands Orthopædic Hospital, Rawdon (100 Beds) and Orthopædic Outpatient Department, Bradford Royal Infirmary. Offers excellent training in all branches of accident and orthopædic surgery. Resident—detached furnished house, suitable for married person ; also single accommodation available.

(*b*) Harrogate General Hospital (38 orthopædic beds). Non-resident.

Psychiatry

(*a*) Menston Hospital, near Leeds (2500 Beds). Residential accommodation can be provided for a single person. If desired, facilities for attendance at the University at Leeds will be provided if the successful candidate is studying for the D.P.M.

(*b*) Storthes Hall Hospital, Huddersfield (2750 Beds). Facilities for attendance at the Leeds University will be provided if the successful candidate is studying for the D.P.M.

Pædiatrics

Bradford A and B Groups. Duties mainly at Children's Hospital (52 Beds). Resident.

Urology

Bradford Royal Infirmary (65 urology beds). Approximately one-fifth of the duties will be general surgical. Non-resident.

General Medicine

Regional Rheumatism Centre, Harrogate (240 Beds), 9 sessions, and Rheumatism Clinic, General Infirmary, Leeds, 2 sessions. Resident at the Royal Bath Hospital, Harrogate.

Applications, stating age, qualifications and details of present and previous appointments with dates, together with the names and addresses of 3 referees, to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 20th August, 1958.

LINCOLN COUNTY HOSPITAL, Sewell-road, Lincoln. (200 Beds.) Applications are invited for the post of RESIDENT HOUSE PHYSICIAN, Male or Female. This is an approved pre-registration post. If satisfactory, this post will be followed by appointment for a second 6 months as House Surgeon.

Applications, with copy testimonials, should be sent to the Secretary as soon as possible.

LIVERPOOL, 14. BROADGREEN HOSPITAL. Applications are invited for appointment as SENIOR HOUSE OFFICER (medicine) which will become vacant on 1st October, 1958. Salary £819 10s. p.a.

Applications, on forms obtainable from the undersigned, to be returned within 10 days of this advertisement.

H. BLYTHE, Group Secretary.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. ST. PAUL'S EYE HOSPITAL. Applications are invited for a post of SENIOR HOUSE OFFICER in Ophthalmology for the year 1st October, 1958–30th September, 1959.

Apply by 18th August, 1958, on form obtainable from the Secretary, The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. LIVERPOOL MATERNITY HOSPITAL. Applications are invited for a post of RESIDENT REGISTRAR in Pædiatrics for the year from 1st October, 1958, to 30th September, 1959. Annual reappointment thereafter until completion of the normal period of training will be considered without the need for further application.

Apply by 23rd August, 1958, on form obtainable from the Secretary, The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. ST. PAUL'S EYE HOSPITAL. Applications are invited for appointment as Locum SENIOR REGISTRAR in Ophthalmology for any period of 8 weeks between 14th September and 23rd December, 1958.

Apply immediately, stating the period for which available, on form obtainable from the Secretary, The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

LOUTH, LINCOLNSHIRE. COUNTY HOSPITAL. (215 Beds.) GRIMSBY HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (surgical), vacant middle of August, 1958, at this General Hospital.

Applications, giving full details, together with the names of 2 referees, should be addressed to the Hospital Secretary.

LOUTH, LINCOLNSHIRE. COUNTY HOSPITAL. (215 Beds.) GRIMSBY HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (surgical). Applications are invited for this pre-registration post, vacant middle of August, 1958.

Applications, giving full details, together with the names of 2 referees, should be addressed to the Hospital Secretary.

LOWESTOFT AND NORTH SUFFOLK HOSPITAL, LOWESTOFT, SUFFOLK. SENIOR HOUSE SURGEON (resident) required. Furnished flat available for married officer, if desired. Post recognised for final F.R.C.S. examination requirements. The Hospital has a Consultant General Surgeon and is regularly visited by Consultants in all specialties from the Norfolk and Norwich Hospital. Membership of a Medical Defence Society is a condition of appointment.

Applications, stating age, qualifications and experience, with names and addresses of 2 referees, to Hospital Secretary.

MANCHESTER. BOOTH HALL CHILDREN'S HOSPITAL, BLACKLEY, MANCHESTER 9. (380 Beds.) Applications are invited for the post of RESIDENT CLINICAL PATHOLOGIST, Senior House Officer grade, which will become vacant during August, 1958. The post, which is tenable for 1 year, affords opportunities for training in all branches of pathology. Candidates should have held house appointments, but previous experience in pathology is not essential.

Application form from Group Secretary.

MANCHESTER REGIONAL HOSPITAL BOARD. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. WYTHENSHAWE HOSPITAL, MANCHESTER, 23. The Board invite applications from registered practitioners for the post of MEDICAL REGISTRAR at the above Hospital.

Applications, stating age, qualifications, present post, experience, and the names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, immediately.

MANCHESTER REGIONAL HOSPITAL BOARD. Resi-DENT SURGICAL REGISTRAR required 1st November, 1958, for the Royal Infirmary, Blackburn, a busy acute hospital of 262 Beds. Post recognised for F.R.C.S.

Application forms available for Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

MANCHESTER REGIONAL HOSPITAL BOARD invites applications for post RESIDENT or NON-RESIDENT ORTHOPÆDIC REGISTRAR to Macclesfield District Group hospitals. Main duties Infirmary Branch, Macclesfield Hospital. To include visits to other hospitals in the Group. Hospital recognised for F.R.C.S. regulations.

Apply immediately, with names and addresses of 2 referees, to Group Secretary, Willerby House, Cumberland-street, Macclesfield.

MANCHESTER REGIONAL HOSPITAL BOARD. Applications are invited for the post of SURGICAL REGISTRAR at the North Lonsdale Hospital, Barrow-in-Furness. The post may be resident or non-resident, as desired, but single residential accommodation only is available. Recognised for F.R.C.S. Available beginning of September.

Applications should be addressed to the Group Secretary, Barrow and Furness Hospital Management Committee, 105, Abbey-road, Barrow-in-Furness.

MANCHESTER. WEST MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. PARK HOSPITAL, DAVYHULME. (General Hospital—433 Beds.) SENIOR HOUSE PHYSICIAN (pædiatrics) required. Previous experience essential. There is a midwifery unit of 73 Beds and a pædiatric unit which includes 10 thoracic surgical beds. Recognised for D.C.H. Post vacant end of September.

Applications, together with names and addresses of 2 referees, to be forwarded to the Group Secretary.

MANCHESTER, 23. WYTHENSHAWE HOSPITAL. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of CASUALTY OFFICER (Junior Hospital Medical Officer grade) at the above Hospital.

Applications, stating age, qualifications, present post, and names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, within 7 days of the appearance of this advertisement.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL EYE HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER.

Application forms may be obtained from the undersigned.

H. R. NORTH, General Superintendent.

Manchester Royal Eye Hospital.

MANCHESTER. UNITED MANCHESTER HOSPITALS, SAINT MARY'S HOSPITALS, MANCHESTER. Applications are invited for 3 posts of SENIOR HOUSE OFFICER in Gynæcology. Applicants must have had previous hospital experience in medicine and surgery. The posts are recognised for the purpose of the M.R.C.O.G. examination. The appointments are for 6 months starting 1st October, 1958. Salary in accordance with national scale.

Application forms may be obtained from the undersigned and returned not later than 18th August, 1958.

A. R. WISE,
General Superintendent, Saint Mary's Hospitals.
Whitworth Park, Manchester, 13.

MEXBOROUGH. MONTAGU HOSPITAL AND ANNEXE. (198 Beds.) Locum SENIOR HOUSE OFFICER (casualty and orthopædics) required.

Applications to the Secretary to the Committee, "Fern Bank", Doncaster-road, Rotherham.

NEWBURY DISTRICT HOSPITAL, Newbury, Berkshire. Locum RESIDENT SURGICAL OFFICER (Senior House Officer grade) required for period 1st–14th September, 1958.

Applications to Secretary.

NEWCASTLE REGIONAL HOSPITAL BOARD. Special AREA OF CUMBERLAND AND NORTH WESTMORLAND. E.N.T. REGISTRAR. Post recognised for F.R.C.S. and D.L.O. Single quarters available at Cumberland Infirmary, Carlisle. Registrar will work under direction of Senior E.N.T. Surgeon at hospitals in Carlisle, West Cumberland, and Dumfries.

Applications, stating age, qualifications and experience, together with names of 3 referees, should be sent to the Senior Administrative Medical Officer, 72, Warwick-road, Carlisle, within 14 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. West Cumberland Group of hospitals. REGISTRAR SURGEON (whole-time) for General Surgery at Workington Infirmary (170 Beds). The appointee will work under the direction of the 2 Consultant Surgeons. A wide variety of elective major surgery is undertaken, also major emergency surgery and casualty work. Appointment for 1 year in the first instance and may be continued for a further year. Post recognised for F.R.C.S. Married quarters available.

Applications, with names and addresses of 3 referees, to be sent to Senior Administrative Medical Officer, 72, Warwick-road, Carlisle, within 14 days.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the non-resident appointment of MEDICAL REGISTRAR at the Royal Victoria Infirmary. The post will offer scope to prepare for a higher degree. The appointment is for 1 year in the first instance and will be subject to the terms and conditions of service of hospital medical staff in the National Health Service.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.
Royal Victoria Infirmary, Newcastle upon Tyne.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for 2 non-resident whole-time appointments of SENIOR HOUSE OFFICER in a General Medical Clinic at the Royal Victoria Infirmary. The appointments are for 1 year and will be subject to the terms and conditions of service of hospital medical staff in the National Health Service. The salary will be at the rate of £819 10s. p.a., subject to the appropriate deductions.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.
Royal Victoria Infirmary, Newcastle upon Tyne.

NORTHAMPTON (near). CREATON HOSPITAL. Applications are invited from suitably qualified medical practitioners for the post of SENIOR HOUSE OFFICER. The Hospital has 138 Beds, and is for the treatment of both pulmonary and non-pulmonary tuberculosis. There is a major thoracic surgical unit for tuberculosis and non-tuberculous diseases of the chest.

Applications, stating age, experience and qualifications, together with the names and addresses of 2 referees, should be sent to the Secretary, Northampton and District Hospital Management Committee, General Hospital, Northampton, within 7 days of the appearance of this advertisement.

NORTH WEST METROPOLITAN REGIONAL HOS-PITAL BOARD. Applications are invited for the post of REGISTRAR in the Geriatric Department of the West Herts Group. Resident or non-resident. Majority of the beds in general hospitals at Watford and Hemel Hempstead with full laboratory and radiological facilities. This post, which is in the charge of a Consultant, offers good clinical experience in the diagnosis and treatment of acute and other diseases of the elderly.

Application forms obtainable from and returnable to the Group Secretary, West Herts Group Hospital Management Committee, 9, Rickmansworth-road, Watford, Herts, by not later than 19th August, 1958.

NUNEATON. MANOR HOSPITAL. (125 Beds.) Regis-TRAR (orthopædic and general surgery). Recognised F.R.C.S. Experience in specialty essential. Resident. Furnished flat available.

Application forms from Group Secretary, Coventry and Warwickshire Hospital, Stoney Stanton-road, Coventry, to be returned by 18th August, 1958.

NOTTINGHAM GENERAL HOSPITAL. Senior House OFFICER (anæsthetics) required 31st August, 1958. The post is recognised for the D.A. and the F.F.A. R.C.S. This is a busy general hospital giving experience in all branches of surgery.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary.

NOTTINGHAM GENERAL HOSPITAL. Senior House OFFICER (surgery) required. Duties to commence immediately.

Applications, stating age, qualifications, experience and nationality, together with copies of testimonials, to be sent to Group Secretary, General Hospital, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. 2 House Sur-GEONS. Pre-registration. Duties to commence as soon as possible.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to Group Secretary.

NOTTINGHAM CITY HOSPITAL. (811 Beds.) Sheffield REGIONAL HOSPITAL BOARD. Whole-time REGISTRAR (thoracic surgery) required. Single accommodation available. Appointment for 1 year in first instance. Thoracic Unit at City Hospital undertakes non-tuberculous and cardiological cases; tuberculosis surgery undertaken at modern unit in nearby Sanatorium, appointee encouraged to attend. Previous thoracic surgical experience desirable.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 18th August, 1958, giving age, nationality, present and previous appointments with dates, naming 3 referees.

NOTTINGHAM CITY HOSPITAL. (811 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (general surgery) vacant 16th September, 1958. The post is approved for the F.R.C.S. The officer appointed will also be required to undertake certain duties in the Orthopædic Department. A deduction of £150 p.a. will be made for residential emoluments.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

OLDHAM AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of Locum SENIOR HOUSE OFFICER (general surgery). Vacant immediately, with duties at the Oldham Royal Infirmary and/or the Oldham and District General Hospital. The appointment will be tenable for a period of approximately 6 months.

Applications, quoting full particulars of qualifications and experience, together with the names and addresses of 2 referees, should be sent immediately to the Group Secretary, Oldham and District Hospital Management Committee, Central Offices, Rochdale-road, Oldham.

ORPINGTON HOSPITAL, Orpington, Kent. Pre-regis-tration HOUSE OFFICER for Orthopædics and E.N.T. Post now vacant offers good experience in large general hospital; pleasantly situated within easy reach of London.

Apply immediately to Surgeon-Superintendent (Orpington 27050).

PAISLEY. ROYAL ALEXANDRA INFIRMARY. House SURGEONS (general) required for above Infirmary as from 1st August, 1958. Posts approved for pre-registration practitioners and F.R.C.S.

Applications to Group Medical Superintendent.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL, Greenbank-road. HOUSE SURGEON, pre-registration post, vacant immediately.

Apply, with names of 3 referees, also stating age, nationality, qualifications and experience, to the Group Secretary.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE.

Royal Portsmouth Hospital (104 orthopædic beds)
ORTHOPÆDIC HOUSE OFFICER (pre-registration). Vacant now.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be forwarded as soon as possible to E. H. HURST, St. Mary's Hospital, Milton-road, Portsmouth.

PRESTON ROYAL INFIRMARY. (400 Beds.) Post- or Pre-registration HOUSE SURGEON. Post vacant mid-August. Recognised for F.R.C.S.

Applications, with names of 2 referees, to Group Secretary, Preston and Chorley Hospital Management Committee, Royal Infirmary, Preston.

READING. BATTLE HOSPITAL. (391 Beds.) Reading AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of RESIDENT JUNIOR HOUSE SURGEON (pre- or post-registration) required in the Accident and Orthopædic Department. F.R.C.S. recognised. Also casualty duties. Vacant immediately.

Apply, stating age, qualifications with dates, nationality, present post, with copy of recent testimonial, to Secretary.

READING. ROYAL BERKSHIRE HOSPITAL. (337 Beds.) Applications are invited from registered and provisionally registered medical practitioners for the resident post of HOUSE PHYSICIAN in the Paediatric Department, vacant 1st September, 1958, and tenable for 6 months.

Write, stating age, qualifications with dates, nationality, present post, with copies of 2 recent testimonials, to Secretary, Royal Berkshire Hospital, Reading.

READING. ROYAL BERKSHIRE HOSPITAL. Applications are invited from registered and provisionally registered medical practitioners for 2 posts as RESIDENT HOUSE PHYSICIAN, vacant 1st September, 1958, and tenable for 6 months.

Write, stating age, qualifications with dates, nationality, present post, with copies of 2 recent testimonials, to Secretary, Royal Berkshire Hospital, Reading.

RICHMOND, SURREY. ROYAL HOSPITAL. Senior HOUSE OFFICER (resident) for Casualty and Orthopædics required 1st September for busy General Hospital of 121 Beds with full Consultant staff. Recognition being sought for F.R.C.S.

Apply, giving age, qualifications, experience, and names of 2 referees, to the Administrative Officer.

RICHMOND, SURREY. ROYAL HOSPITAL. Senior HOUSE SURGEON (resident) required 1st September for busy General Hospital of 121 Beds with full Consultant staff. Recognition for F.R.C.S. being sought.

Apply, giving age, qualifications, experience, and names of 2 referees, to the Administrative Officer immediately.

REDHILL. EAST SURREY HOSPITAL, Shrewsbury-road, REDHILL, SURREY. RESIDENT HOUSE SURGEON (Male). Pre-registration appointment vacant immediately. Opportunity of House Physician's post to follow if required.

Applications to Hospital Secretary.

ROCHDALE AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN required at Birch Hill Hospital. Resident post now available.

Apply at once to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, Lancs.

ROCHDALE AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (surgical) required immediately for busy Surgical Unit. Post recognised for F.R.C.S. qualification and offering excellent experience.

Apply at once to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, Lancs.

ROCHDALE GROUP OF HOSPITALS. Locum Junior HOSPITAL MEDICAL OFFICER (anæsthetics) required immediately. 6 months' appointment.

Apply at once to the Group Secretary, Birch Hill Hospital, Rochdale.

ROCHFORD, ESSEX. GENERAL HOSPITAL. Locum PATHOLOGICAL REGISTRAR required at the General Hospital, Rochford, on a month-to-month basis. Single accommodation available, if required. Post vacant immediately.

Apply to the Secretary as soon as possible.

ROCHFORD, ESSEX. GENERAL HOSPITAL. (620 Beds.) SENIOR HOUSE OFFICER (surgery) required. Post recognised for F.R.C.S., and is resident. Vacant approximately 24th August.

Applications, stating age, &c., to reach the Secretary by 16th August, 1958.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) RESIDENT HOUSE SURGEONS (2) required from 24th August and 10th September, 1958, respectively, in the General Surgical Unit. Recognised for F.R.C.S. Open to either pre-registration applicants or to fully registered practitioners. This very active Unit of a total of approximately 180 Beds affords ample opportunities for candidates to obtain first-class tuition and experience. The candidates appointed will be attached to a unit of approximately 60 Beds.

Apply immediately to Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) ORTHOPÆDIC HOUSE SURGEON (resident) required in the Orthopædic and Accident Unit. The service consists of 100 Beds equally divided between traumatic surgery and "cold" orthopædics. Post is recognised for pre-registration purposes and for F.R.C.S.

Applications to be sent to Group Secretary, Romford Hospital Management Committee, Oldchurch Hospital, as soon as possible.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. Resident PATHOLOGIST (Senior House Officer grade). This post, which will become vacant on 1st October, 1958, provides valuable experience by rotation through all departments of this large Group Laboratory and is recognised for the purposes of the Diploma in Pathology. Prospective candidates are invited to visit the laboratory.

Applications should be sent with testimonials or the names of 2 referees, before 18th August, 1958, to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROMFORD. RUSH GREEN HOSPITAL. Locum MEDICAL REGISTRAR required immediately for period of 3–6 months. Male or Female. Resident or non-resident.

Apply at once to Medical Superintendent. Telephone: Romford 46066.

RUGBY. HOSPITAL OF ST. CROSS. House Surgeon in General Surgery (pre-registration). Recognised F.R.C.S. Resident.

Applications to Hospital Secretary.

SALFORD, 6, LANCASHIRE. HOPE HOSPITAL. Salford HOSPITAL MANAGEMENT COMMITTEE. 2 RESIDENT HOUSE SURGEONS (post- or pre-registration), required at the above Hospital. These posts are recognised for the F.R.C.S.

Applications, stating age, qualifications and experience, together with the names and addresses of 2 referees, should be forwarded to the Hospital Secretary immediately.

SALISBURY GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of PÆDIATRIC REGISTRAR/RESIDENT MEDICAL OFFICER at Odstock Hospital for a period of 12 months in the first instance from 17th October, 1958.

Application forms may be obtained from, and must be returned to, the Group Secretary, Odstock Hospital, Salisbury, by 20th August.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance :—

SENIOR REGISTRAR in Pathology based at Gateside Infectious Diseases Hospital, Greenock.

SENIOR REGISTRAR in Bacteriology based at the Royal Alexandra Infirmary, Paisley.

REGISTRAR in Pathology based at the Royal Infirmary, Glasgow.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 23rd August, 1958.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications invited for the following posts :—

(*a*) RESIDENT SURGICAL OFFICER (Registrar grade) at the Royal Hospital. Vacant 1st September. Post is ideal for candidates working for final F.R.C.S. The holder acts as Registrar to a general surgical firm. Closing date for applications 12th August.

(*b*) REGISTRAR in E.N.T. Surgery, to the Royal Infirmary and Children's Hospital. Post vacant 1st October. Closing date for applications 23rd August.

Applications for the above posts, with names of 3 referees, to the Chief Administrative Officer, United Sheffield Hospitals, West-street, Sheffield, 1.

SHOREHAM-BY-SEA, SUSSEX. SOUTHLANDS HOSPITAL. Applications are invited for the appointment of RESIDENT HOUSE PHYSICIAN/HOUSE SURGEON to run consecutively for a period of 6 months in each post. Posts approved for pre- or post-registration practitioners and F.R.C.S.

Applications to Hospital Secretary, Southlands Hospital, Shoreham-by-Sea. A. V. OAKTON, Group Secretary, Worthing Group Hospital Management Committee.

SHREWSBURY. CROSS HOUSES HOSPITAL. Obstetric HOUSE SURGEON. Pre-registration post. Vacant 1st September, 1958.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. EYE, EAR AND THROAT HOSPITAL. SENIOR HOUSE OFFICER (E.N.T.). Duties at E.N.T. Hospital (68 Beds) and Copthorne Hospital (168 Beds). Post recognised for the D.L.O. R.C.S. and F.R.C.S. Vacant immediately.

Applications, with copy testimonials, to the Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY/COPTHORNE HOSPITAL. (500 Beds.) HOUSE SURGEON. Vacant immediately. Pre-registration candidates eligible. Recognised for the F.R.C.S.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SOUTHAMPTON GROUP HOSPITAL MANAGEMENT COMMITTEE, Bullar-street, SOUTHAMPTON. Locum ANÆSTHETIC REGISTRAR required immediately for a period of 6–8 weeks.

Applications to Group Secretary as soon as possible.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of 2 REGISTRARS in Psychiatry to the Brighton and Lewes Group of hospitals. 1 appointment is for the Psychogeriatric Unit at Brighton General Hospital, where a Consultant Geriatrician and a Consultant Psychiatrist both attend, and will also include general duties in other geriatric blocks at this Hospital, and in the long-stay wards. The other appointment is for duties in the Observation Unit at the same Hospital, which will include signing extensions of orders under the Lunacy and Mental Treatment Acts. After 6 months opportunities might be offered for the successful candidate for the Observation Unit post to work in St. Francis Hospital, Haywards Heath. The holders of the 2 appointments will be expected to undertake complete psychiatric/geriatric relief duties for each other. Both successful candidates should be resident at Brighton General Hospital. The appointments will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales) and will be for 1 year in the first instance,

Applications, indicating for which appointment(s) candidates wish to be considered, giving particulars of age, qualifications and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, 11, Portland-place, W.1, not later than 23rd August, 1958.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Obstetrics and Gynæcology to fill a vacancy in the approved trainee establishment at the Bromley Group of hospitals, available on 1st November, 1958. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, 11, Portland-place, W.1, not later than 23rd August, 1958.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as REGISTRAR in Neurosurgery at the Neurosurgical Unit at Hurstwood Park Hospital, Haywards Heath, Sussex. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 23rd August, 1958.

SOUTHPORT GENERAL INFIRMARY. (189 Beds. Recognised for pre-registration and F.R.C.S.) HOUSE SURGEON (general surgery and gynæcology). Post vacant now.

Apply, with 2 copy testimonials, to Group Secretary, Southport and District Hospital Management Committee, Promenade Hospital, Southport.

SOUTHEND-ON-SEA. GENERAL HOSPITAL. Locum SENIOR SURGICAL REGISTRAR required for the period 25th August–13th September, 1958, or 1st–20th September, 1958, inclusive.

Applications, &c., to be sent to the undersigned immediately.

J. C. FIELD, Secretary.

SOUTHEND. GENERAL HOSPITAL. House Surgeon required for General Surgery and E.N.T. Resident post. Some duties at Victoria Hospital, Westcliff.

Applications as soon as possible to the Secretary.

ST. ALBANS, HERTFORDSHIRE. CELL BARNES HOSPITAL. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required at above Hospital. This is a modern Hospital where 895 mental defectives of all types and ages are under care. Approved for D.P.M. Good pædiatric experience available. Hospital may be visited by direct appointment.

Application forms obtainable from the Group Secretary, Harperbury Hospital, St. Albans, Hertfordshire, and returnable by 26th August, 1958.

ST. ALBANS, HERTFORDSHIRE. CELL BARNES HOSPITAL. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. JUNIOR HOSPITAL MEDICAL OFFICER required at above Hospital. This is a modern Hospital where 895 mental defectives of all types and ages are under care. Approved for D.P.M. Good pædiatric experience available. Hospital may be visited by direct appointment.

Application forms obtainable from the Group Secretary, Harperbury Hospital, St. Albans, Herts, and returnable by 26th August, 1958.

ST. ASAPH HOSPITAL, St. Asaph, Flintshire. Appointment of HOUSE OFFICER. Duties divided between ophthalmology (16 Beds), E.N.T. (12 Beds), and oral surgery (4 Beds).

Applications, stating age, qualifications and experience, accompanied by 2 recent testimonials, to be sent forthwith to the Group Secretary, Clwyd and Deeside Hospital Management Committee, "Rhianfa", Russell-road, Rhyl.

ST. HELENS AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. WHISTON HOSPITAL, PRESCOT. (892 Beds.) (Obstetrical Unit 74 Beds.) Applications are invited for the resident post of SENIOR HOUSE OFFICER (obstetrics and gynæcology), which is recognised for the M.R.C.O.G. and D.Obst.R.C.O.G. examinations. Previous obstetrical and gynæcological experience is essential.

Applications, stating age, qualifications, experience and nationality, and giving 2 names for reference, should be forwarded to N. RICHARDS, Group Secretary, Whiston Hospital, Prescot.

ST. LEONARD'S HOSPITAL, Nuttall-street, London, N.1. Applications are invited from registered or provisionally registered medical practitioners for the post of HOUSE SURGEON for 6 months.

Apply immediately, with 2 recent testimonials, to Hospital Secretary.

STOCKPORT. STEPPING HILL HOSPITAL. (529 Beds.) Applications are invited for 2 pre-registration posts of HOUSE OFFICER (medicine), 1 post vacant now and the other on 21st August, 1958.

Applications, with full particulars and names of 2 persons for reference, to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport.

STOCKPORT. STEPPING HILL HOSPITAL. (529 Beds.) Applications are invited for the post of HOUSE OFFICER (general surgery).

Applications, with copies of 2 testimonials, to the Group Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. (815 Beds.) STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN (general medicine—pre-registration appointment) required. The post offers wide experience in general medicine and cardiology.

Applications to the Hospital Secretary.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. (815 Beds.) STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (general surgery) required immediately. The post offers wide experience in general, thoracic and cardiac surgery. No casualty work. Recognised for the F.R.C.S.

Applications to the Hospital Secretary.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. HOUSE OFFICER (general surgery) required. Recognised for F.R.C.S. Post vacant very shortly.

Detailed applications, with copy testimonials, to Hospital Secretary, North Staffordshire Royal Infirmary, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. HOUSE PHYSICIAN (general medicine and dermatology) required. Pre-registration post. Post vacant very shortly.

Detailed applications, with copy testimonials, to Hospital Secretary, North Staffordshire Royal Infirmary.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. HOUSE PHYSICIAN (general medicine and pædiatrics) required. Pre-registration post, vacant very shortly.

Detailed applications, with copy testimonials, to Hospital Secretary, North Staffordshire Royal Infirmary, Stoke-on-Trent.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL, PEMBURY, KENT. (357 Beds.) TUNBRIDGE WELLS GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for pre-registration post of HOUSE SURGEON. 6 months' appointment. Vacant now.

Apply, giving details of age, experience and qualifications, to Surgeon-Superintendent.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL. (357 staffed available beds.) TUNBRIDGE WELLS GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for post of HOUSE PHYSICIAN (Senior House Officer) in Pædiatric Unit. Vacant 1st October, 1958. Previous pædiatric experience desirable. Post tenable for 12 months and recognised for D.C.H. examination.

Apply, stating age, qualifications and experience, with 3 recent testimonials, by 30th August, to Group Secretary, Tunbridge Wells Group Hospital Management Commitee, Sherwood Park, Pembury-road, Tunbridge Wells.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL, PEMBURY, KENT. (357 Beds.) TUNBRIDGE WELLS GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for pre-registration post of ORTHOPÆDIC HOUSE SURGEON. 6 months' appointment. Vacant now.

Apply, giving details of age, experience and qualifications, to Surgeon-Superintendent.

TAUNTON AND SOMERSET HOSPITAL, Taunton, SOMERSET. Applications are invited for the post of SENIOR HOUSE OFFICER (casualty and orthopædic).

Applications, stating age, nationality and qualifications, together with the names of 2 referees, should be forwarded to the Group Secretary, Taunton Hospital Management Committee, c/o Musgrove Park Hospital, Taunton.

TAUNTON AND SOMERSET HOSPITAL, Taunton, SOMERSET. HOUSE OFFICER (general surgery) required. Pre-registration post recognised for F.R.C.S., vacant now.

Applications, stating age, nationality and qualifications, to the Group Secretary, Taunton Hospital Management Committee, c/o Musgrove Park Hospital, Taunton.

WAKEFIELD. CLAYTON HOSPITAL. (207 Beds.) HOUSE SURGEON (general surgery and orthopædics) required at above Hospital. Approved pre-registration appointment.

Application forms obtainable from the Group Secretary, Hospital Management Committee, No. 9 Wakefield A Group, 113, Northgate, Wakefield.

WAKEFIELD. PINDERFIELDS GENERAL HOSPITAL. (Regional Thoracic Centre.) Applications invited for positions of SENIOR HOUSE PHYSICIAN and SENIOR HOUSE SURGEON. Salary £819 10s. p.a. £150 p.a. charged for accommodation.

Address written applications, giving full personal particulars, details of experience and 2 names and addresses for reference, to W. BOWRING, Group Secretary, Pinderfields General Hospital, Wakefield.

WAKEFIELD. PINDERFIELDS GENERAL HOSPITAL. SENIOR HOUSE OFFICER required for the Orthopædic Department. Salary £819 10s. p.a., £150 p.a. charged for accommodation.

Address written applications, giving full particulars of experience and 2 names and addresses for reference, to W. BOWRING, Group Secretary, Pinderfields General Hospital, Wakefield.

WAKEFIELD. STANLEY ROYD HOSPITAL. Applications invited for post of JUNIOR HOSPITAL MEDICAL OFFICER or SENIOR HOUSE OFFICER in Psychiatry. Accommodation available for a single person.

Address written applications, giving full personal particulars, details of training, experience, &c., and 2 names and addresses for reference, to W. BOWRING, Group Secretary, Pinderfields General Hospital, Wakefield.

WALSALL HOSPITAL MANAGEMENT COMMITTEE. Locum HOUSE SURGEON and HOUSE PHYSICIAN required for the General (Sister Dora) Hospital and the Manor Hospital.

Apply Group Secretary, Walsall General (Sister Dora) Hospital.

WARRINGTON GENERAL HOSPITAL. (344 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST (Male or Female), graded as Senior House Officer. The Hospital is recognised for the D.A. examination. Salary is £819 10s. p.a., less a deduction of £150 p.a. for residential emoluments.

Applications, stating qualifications and experience, should be sent to HENRY L. BOOT, Group Secretary, Warrington and District Hospital Management Committee, c/o General Hospital, Warrington, Lancs.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. (211 Beds.) Applications are invited for the post of HOUSE SURGEON at the above Hospital. This is a pre-registration post and is recognised for F.R.C.S. Salary according to the National Health Service scale. Post vacant now.

Please send copies of recent testimonials, with applications, to the Administrator.

WATFORD HOSPITALS. North West Metropolitan REGIONAL HOSPITAL BOARD. ANÆSTHETIC REGISTRAR (resident) required for the above Hospitals. Application made for recognition. Post vacant immediately.

Application forms obtainable from and returnable to Secretary, West Herts Group Hospital Management Committee, 9, Rickmansworth-road, Watford, Herts, by 19th August, 1958.

WESTON-SUPER-MARE GENERAL HOSPITAL. (104 Beds.) Applications are invited from duly qualified medical practitioners for the pre-registration appointment (resident) of HOUSE SURGEON. Immediate vacancy.

Applications, stating age, qualifications, together with names and addresses of 2 referees, should be addressed to the Group Secretary, Weston-super-Mare Hospital Management Committee.

WESTON-SUPER-MARE GENERAL HOSPITAL. (104 Beds.) SENIOR HOUSE OFFICER (surgical) required at above Hospital. Immediate vacancy. Single residential accommodation available.

Applications, stating age, qualifications and experience, together with names and addresses of 2 referees, should be addressed to Group Secretary, Weston-super-Mare Hospital Management Committee.

WHITEHAVEN HOSPITAL, Cumberland. (122 Beds, plus 31 Beds in Annexe.) HOUSE SURGEON, with orthopædic and casualty duties (recognised pre-registration, Senior House Officer grade if appropriate). Vacant beginning of September.

Detailed applications, with dates, names of 2 referees, to Group Secretary, Workington Infirmary, Cumberland.

WIGAN AND LEIGH HOSPITAL MANAGEMENT COMMITTEE. LEIGH INFIRMARY, LEIGH. SENIOR HOUSE OFFICER required for Casualty Department, with gynæcological and surgical duties at Astley Hospital. Resident post. Vacant now.

Apply Secretary, Knowsley House, Wigan.

WIGAN AND LEIGH HOSPITAL MANAGEMENT COMMITTEE. WHELLEY HOSPITAL. (71 acute medical beds.) HOUSE PHYSICIAN, pre-registration post.

Applications, with names of 2 referees, to Secretary, Knowsley House, Wigan.

WINCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR in Anæsthetics (Registrar grade) required at the Royal Hampshire County Hospital, Winchester, with duties in the Lord Mayor Treloar Group, Alton. Post recognised for the F.F.A. R.C.S. and is resident or non-resident.

Forms of application obtainable from Group Secretary, Royal Hampshire County Hospital, Winchester.

WINDSOR. KING EDWARD VII HOSPITAL. Registrar (Casualty Officer), resident or non-resident, required immediately. There is an accident unit of 30 Beds at the Hospital, and with the Casualty Department forms part of the Accident Service for the Windsor Group and includes duties with the E.N.T. and Eye Departments. Candidates should have had previous experience in the treatment of acute injuries.

Application forms from and returnable to Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor.

WOKING AND CHERTSEY GROUP LABORATORY. Applications invited for post of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer). The post is 1 of 2, and involves a half share in emergency service. Training available in all branches of clinical pathology. Post tenable for 1 year from mid-September. Salary £819 10s. p.a.

Applications, stating age, qualifications, &c., together with names of 2 referees, as soon as possible to the Director, Group Laboratory, St. Peter's Hospital, Chertsey, Surrey.

WOLVERHAMPTON. NEW CROSS HOSPITAL. (634 Beds.) HOUSE OFFICER (pre-registration), Medicine. Acute medical beds. Vacant now.

Applications to Hospital Secretary.

WOLVERHAMPTON. NEW CROSS HOSPITAL. Pre-registration HOUSE OFFICER in General Surgery. Post recognised for F.R.C.S.

Applications to Hospital Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An associated hospital of the Birmingham University Medical School.) HOUSE OFFICER (pre-registration) E.N.T. Department. Post recognised for the D.L.O. and F.R.C.S. examinations. Vacant 10th September.

Apply, with copies of 2 testimonials, to the Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. House SURGEON for Thoracic Surgery and Casualty. Post recognised for F.R.C.S. Vacant immediately.

Apply, with 2 testimonials, to Secretary.

WREXHAM. MAELOR GENERAL HOSPITAL (591 Beds) AND WAR MEMORIAL HOSPITAL, WREXHAM (230 Beds). Applications are invited for HOUSE PHYSICIAN and SURGEON posts at the above Hospitals to commence immediately. The appointments are recognised for pre-registration purposes.

Applications, stating age, nationality, qualifications and experience, together with copies of 2 recent testimonials, should be addressed to the Group Secretary, Wrexham, Powys and Mawddach Hospital Management Committee, Maelor General Hospital, Wrexham, Denbighshire.

WREXHAM. MAELOR GENERAL HOSPITAL. (591 Beds.) Applications are invited for the post of PÆDIATRIC HOUSE PHYSICIAN at the above Hospital, to commence immediately. The appointment is recognised for the D.C.H. and for pre-registration purposes.

Applications, stating age, nationality, qualifications and experience, together with copies of 2 recent testimonials, should be addressed to the Group Secretary, Wrexham, Powys and Mawddach Hospital Management Committee, Maelor General Hospital, Wrexham, Denbighshire.

YORK. COUNTY, CITY, MILITARY (Civilian Wing), AND FULFORD HOSPITALS. (General Hospitals of 266, 256, 60, and 149 Beds respectively, with full Consultant staff.) SENIOR HOUSE OFFICER in Anæsthetics, resident or non-resident, required. Post is recognised for F.F.A. R.C.S. and D.A. Previous experience desirable but not essential. Vacant from 1st October, 1958.

Applications, stating age, nationality, qualifications, experience and names of 2 referees, to Group Secretary, York A and Tadcaster Hospital Management Committee, Bootham Park, York.

YORK. COUNTY HOSPITAL. (General, 266 Beds.) CITY HOSPITAL, YORK. (General, 256 Beds.) Locum Tenens HOUSE SURGEONS required for the above Hospitals immediately.

Applications, giving full particulars and names of 2 referees, to Group Secretary, York A and Tadcaster Hospital Management Committee, Bootham Park, York.

AUSTRALIA. GIPPSLAND BASE HOSPITAL, City of SALE, VICTORIA, AUSTRALIA. Vacancies exist for the appointment of 2 fully registered JUNIOR MEDICAL OFFICERS in this regional hospital. Training facilities available in medicine, surgery, midwifery, gynæcology and pædiatrics. Salary to commence £800 sterling rising in 2 annual increments of £100 sterling. Contract for 3 years initially with possibilities of extension. Free residential emoluments for single and married applicants with married quarters available. Excellent opportunities in general practice.

Applications and inquiries directed to E. C. SPEECHLEY, Secretary and Superintendent.

CHANNEL ISLANDS. JERSEY GENERAL HOSPITAL. (200 Beds—D.A. recognised.) Applications are invited for the position of RESIDENT SENIOR HOUSE OFFICER for anæsthetic duties. The post falls vacant on 25th September, 1958. The appointment is for 12 months in the first instance. Salary £850 p.a., less £125 for residential emoluments.

Applications to be submitted not later than 27th August, 1958, to the President, Public Health Committee, General Hospital, Jersey, C.I.

ST. JOHN'S, NEWFOUNDLAND, CANADA. GENERAL HOSPITAL. (475 Beds.) Applications are invited for the post of RESIDENT in the Pathology Department of the above Hospital. (There are 3 Residents in this Department.) The post is recognised for postgraduate training towards certification in pathology by The Royal College of Surgeons and Physicians of Canada, and also recognised by the Royal College of Surgeons, England, for the Diploma in Pathology. Excellent opportunities exist for gaining extensive experience. Salary $3200 p.a., less $660 for maintenance, &c. Transport to St. John's will be paid by the Hospital.

Applications, with full details, &c., to be forwarded to Dr. B. WILSON, Superintendent, The General Hospital, St. John's, Newfoundland, Canada.

Hospital Services: Non-Medical Appointments

BIRMINGHAM CHILDREN'S HOSPITAL. Biochemist, preferably with postgraduate experience, required for research into lipoprotein metabolism in childhood diabetes. Post unestablished but could provide opportunity to prepare for higher degree. Salary £550–£1000 according to experience.

Applications to H. B. SALT, Department of Biochemistry, Children's Hospital, Birmingham, 16.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited from suitably qualified persons for the post of SECRETARY to the Board of Governors which becomes vacant on 31st March, 1959, due to the retirement of the present holder. The undergraduate Teaching Hospital scale (£2170–£2671) will be applicable. The Teaching Hospital Group comprises the Royal Victoria Infirmary (680 Beds), the Princess Mary Maternity Hospital (106 Beds), the Babies Hospital (35 Beds), the Dental Hospital, all in Newcastle upon Tyne, and the Castle Hill Convalescent Home (97 Beds) at Wylam. Candidates should possess wide experience in a senior administrative capacity.

Candidates should forward under confidential cover 15 copies of their application, with full details of age, educational qualifications and experience, together with the names of 3 referees, by 20th September, 1958, to the Chairman of the Board of Governors, Royal Victoria Infirmary, Queen Victoria-road, Newcastle upon Tyne, 1.

Public Appointments

MIDDLESEX COUNTY COUNCIL. County Health DEPARTMENT. SENIOR ASSISTANT MEDICAL OFFICER (Male) required initially in Area 6 (Wembley and Willesden). Whole-time for administrative and clinical work. Approval by Minister of Education for ascertainment of educationally subnormal children desirable. Diploma in Public or Child Health advantage. Required to act as Deputy Medical Officer of Health for Borough of Willesden for 40% of whole-time. Salary as for mixed appointments, £1693 13s. 4d.–£2058 13s. 4d. Established, subject to medical assessment. Prescribed conditions.

Apply, stating age, qualifications, experience and names of 2 referees, to Joint Area Medical Officers, 215, Chevening-road, Kilburn, N.W.6, by 23rd August. (Quote X.946L.) Canvassing disqualifies.

BOLTON. COUNTY BOROUGH OF BOLTON. Health DEPARTMENT. Applications are invited from registered medical practitioners for a Locum MEDICAL appointment for a period of about 4 months commencing in mid-October. Duties will consist of attendance at Infant Welfare and School Clinics, conducting of medical examinations and such other clinical duties as may from time to time be required. Salary in accordance with Medical Whitley Council Committee C, viz., £1050–£1475 p.a.

Applications, with names of 2 referees, to Medical Officer of Health, Civic Centre, Bolton, by 16th August.

PHILIP S. RENNISON, Town Clerk.

BUCKINGHAMSHIRE. COUNTY OF BUCKINGHAM-SHIRE. Applications are invited from registered medical practitioners holding the Diploma in Public Health or its equivalent for the joint appointment of MEDICAL OFFICER OF HEALTH for the Amersham Rural, Beaconsfield and Chesham Urban Districts, and DEPUTY DIVISIONAL SCHOOL MEDICAL OFFICER AND ASSISTANT COUNTY MEDICAL OFFICER for the Bucks County Council. The person appointed will be employed for 6/11ths of his time as Medical Officer of Health for the Districts mentioned, and for the remaining 5/11ths as Deputy Divisional School Medical Officer and Assistant County Medical Officer for the Bucks County Council. The combined salary scale will be £1657 0s. 11d., rising to a maximum of £2018 10s. 5d. p.a. Travelling and subsistence allowances will be paid on the appropriate scale. The appointment is superannuable and subject to medical examination.

Further particulars and forms of application can be obtained from the Clerk of the County Council, County Hall, Aylesbury, to whom applications must be delivered by 1st September, 1958.

LEEDS. CITY OF LEEDS. Applications are invited from registered medical practitioners for the combined appointment of DEPUTY MEDICAL OFFICER OF HEALTH AND DEPUTY PRINCIPAL SCHOOL MEDICAL OFFICER. Applicants must possess the qualifications prescribed by the Local Government Act, 1933, and the regulations made thereunder. The duties of the post include that of Deputy Medical Referee to the Municipal Crematorium and the Lawnswood Crematorium. The salary attached to the combined office is £1770 p.a., rising by annual increments of £105 to a maximum of £2085 p.a. The appointment is subject to the Local Government Superannuation Acts, 1937 and 1953, and the successful candidate will be required to pass a medical examination.

Applications, endorsed "Deputy Medical Officer of Health," and giving the names of 3 persons to whom reference can be made, must reach the undersigned not later than 1st September, 1958. Canvassing in any form, either directly or indirectly, will be a disqualification. ROBERT CRUTE, Town Clerk.

Civic Hall, Leeds, 1.

CAMBRIDGESHIRE COUNTY COUNCIL. Applications are invited for the post of COUNTY MEDICAL OFFICER OF HEALTH for the Administrative County of Cambridge from men of not more than 50 years of age who are duly qualified medical practitioners registered in the medical register as holders of a diploma in sanitary science, public health or state medicine. The salary offered is £2500–£105(2)–£55(1)–£2765 p.a., and the post is designated for purposes of superannuation subject to the successful candidate passing a medical examination.

Further particulars and a form of application can be obtained from the Clerk of the Cambridgeshire County Council, Shire Hall, Cambridge. Applications must be received not later than Saturday, 20th September, 1958.

LINDSEY COUNTY COUNCIL. Health Department. Applications invited for post of ASSISTANT MEDICAL OFFICER for Brigg and Barton Area of Lindsey, mainly in connection with examination of school children. Diploma in Public Health an advantage. Salary £1050 rising by 3 increments of £50 and 5 of £55 to a maximum of £1475.

Further particulars and application forms from Dr. C. D. CORMAC, Health Department, County Offices, Lincoln.

MANCHESTER. CITY OF MANCHESTER HEALTH DEPARTMENT. Applications are invited from registered medical practitioners (Male or Female) for the position of MEDICAL OFFICER (Maternity and Child Welfare) on the permanent staff. Applicants should have obstetric and pædiatric experience and will be required to undertake duties principally in Maternity and Child Welfare Clinics. Possession of the D.Obst.R.C.O.G., D.P.H., or D.C.H. will be an advantage. Salary scale £1050 rising to £1475 p.a., the commencing salary depending on previous experience, Medical Council "C" conditions of service.

Application forms may be obtained from the Town Clerk, Town Hall, Manchester, 2, to whom they should be returned within 21 days of the appearance of this advertisement.

GOVERNMENT OF BAHRAIN, MEDICAL DEPARTMENT, BAHRAIN, PERSIAN GULF. The Government of Bahrain invites applications from British lady doctors (age 35–45 years) for the post of ASSISTANT to the Senior Lady Medical Officer. Duties will be general and administrative in a new women's hospital of 210 Beds and other medical units. Preference will be given to an M.R.C.O.G. and interest in midwifery. Salary will range from £1800 to £2520 a year (R.2000 to R.2800 a month) depending on experience and degrees. Annual increments of £90. No allowances. No income-tax, provident fund or pension. Free quarters with hard furniture and transport. Agreement for 2 years, renewable, with 5 months' home leave on full pay and air tourist passages. Appointment from November, 1958.

Write to the Crown Agents, 4, Millbank, London, S.W.1. State age, name in block letters, full qualifications and experience, and quote M3C/44916/LD and enclose photograph.

GOVERNMENT OF THE FEDERATION OF RHODESIA AND NYASALAND. MINISTRY OF HEALTH. As a result of continual expansion further vacancies exist for GOVERNMENT MEDICAL OFFICERS. These are essentially general duty posts and applicants must have completed 1 year's experience since qualifying. Minimum commencing emoluments, including allowances in lieu of private practice, vary between £1550 and £1750 p.a., according to experience. The maximum gross emoluments on this grade are £2250, but opportunities exist for transfer to centres with private practice benefits or promotion to higher grades.

Application forms and further details may be obtained from the Secretary (R), Rhodesia House, 429, Strand, London, W.C.2. Closing date August 23rd.

HER MAJESTY'S OVERSEAS CIVIL SERVICE. BAHAMAS. Applications invited from doctors with qualifications registrable in United Kingdom for appointment as ASSISTANT MEDICAL OFFICER in the Princess Margaret Hospital in Nassau. Liability after first year to serve in Out Islands. Appointment on permanent basis with pension or on agreement for 3 years. (Only permanent officers are members of Her Majesty's Overseas Civil Service.) Salary £1400 a year (but revision under consideration). No income-tax at present. Free quarters if posted to the Out Islands or rent assistance if posted to New Providence. Private practice permitted in Out Islands. Free passages for officer, wife, and up to 2 children on appointment. Free return passages if appointed on agreement. Baggage allowance up to £40 payable on excess baggage. Generous leave. Healthy climate. Excellent social and recreational facilities.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD.117/27/02).

THE NIGERIAN RAILWAY CORPORATION invites applications for the post of DISTRICT MEDICAL OFFICER in the recently formed and expanding Medical Department of the Corporation.

Duties: The District Medical Officer will be in charge of a Railway District Hospital and Dispensaries, and will be responsible for the medical and surgical care of the staff of the Corporation and their families, together with such administrative and public health duties as pertain to effective railway working.

Qualifications: Candidates must be legally qualified medical practitioners, of at least 8 years' experience as such, entitled to practise in Great Britain and possess additional postgraduate medical qualifications and extensive medical experience (both clinical and administrative); the holding of M.R.C.P. or F.R.C.S. is preferred; some administrative experience in the tropics is desirable but not essential.

Salary: £2350 p.a. Appointments may be on pensionable terms or on contract with a gratuity payable on completion of contract at the rate of £39 3s. 4d. for each completed month of service.

Tours: 15 months in Nigeria followed by 15 weeks' leave on full pay.

Quarters: Partly furnished quarters are provided at low rental.

Allowances: There are attractive family, travelling, transport and other allowances.

Send postcard before 20th August, 1958, mentioning the post and this paper, for further particulars and application form to the London Representative, Nigerian Railway Corporation, Nigeria House, 9, Northumberland-avenue, London, W.C.2.

STOKE-ON-TRENT. CITY OF STOKE-ON-TRENT. PUBLIC HEALTH DEPARTMENT. Applications are invited from qualified medical practitioners for the post of ASSISTANT MEDICAL OFFICER on the Maternity and Child Welfare Services. Candidates should have experience in diseases of children and obstetrics. Opportunity will be given for hospital contact with both pædiatrics and obstetrics. The possession of a D.P.H., D.C.H., or D.Obst.R.C.O.G. will be considered an additional qualification. The salary will be at the rate recommended by the Whitley Council, with starting salary according to experience. The appointment will be subject to the provisions of the National Health Services (superannuation) regulations, 1947, and the successful candidate will be required to pass a medical examination.

Forms of application may be obtained from the Medical Officer of Health, Public Health Department, Glebe-street, Stoke-on-Trent, and should be returned, accompanied by copies of not more than 3 recent testimonials.

HARRY TAYLOR, Town Clerk.

General Practice

For an Executive Council post (England and Wales) apply on form E.C.16A obtainable from the council. Mark envelope "Vacancy."

INNERLEITHEN, PEEBLESSHIRE. Applications invited for single-handed semi-rural practice which has become vacant on account of death. List at present 1970. House and surgery will be available for purchase if desired. Applications by 20th August, 1958, stating age, qualifications and experience and names of 2 referees, to the Clerk, Lothians and Peebles Executive Council, 25, Stafford-street, Edinburgh, 3, from whom further information is obtainable.

LIVERPOOL. Childwall Valley. Applications invited in connection with the establishment of a medical practice on a Corporation Housing Estate. There is no list of patients. Accommodation on the Estate will be available. Apply on Form E.C.16A to the undersigned not later than Saturday, 23rd August, 1958.

J. G. DONCASTER, Clerk, Liverpool Executive Council.
36, Princes-road, Liverpool, 8.

OXFORD COUNTY AND CITY. Applications invited for VACANCY (small Rural practice situated North Oxfordshire (near Banbury)). List at present approximately 1062; of these 1032 are dispensing patients. Practice suited to a doctor already established in single-handed practice requiring smaller list. Residence surgery likely to be available. Apply on Form E.C.16A to the undersigned immediately.

V. R. PARRY, Clerk of the Council.
73, George-street, Oxford.

Miscellaneous

The Medical Defence Union. Applications are invited from registered medical practitioners, not exceeding 35 years of age, for appointment as an Assistant Secretary to the Medical Defence Union. The salary scale will range from £1750, rising by annual increments of £50 to £2000 p.a., and the successful applicant will be placed at a point on that scale according to his experience and qualifications for the appointment. The practitioner selected will be required to submit to a medical examination, and to contribute to the Union's superannuation fund.

Applications (12 copies), stating age, qualifications and medical experience, together with the names of 3 persons to whom reference can be made for further information, should reach the Secretary, The Medical Defence Union, Tavistock House South, Tavistock-square, W.C.1, not later than 30th September, 1958.

ASSISTANT

Required Private Mental Hospital of 30 Beds, 8 miles from London, from September or before. Permanent position for suitable colleague, later partnership possible. Male preferred, live in. Need not know anything about psychiatry, but must have makings of dependable physician. Interesting, varied, successful work in a happy, congenial, informal atmosphere.—Address, No. 418, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Christmas Island, Indian Ocean. Applications are invited for the position of Assistant Medical Officer. Applicants should be British born and have a British University Degree. Term of engagement 3½ years. Salary £1450 Australian currency p.a. Free board, or allowance in lieu thereof. Free housing, partial furnishing. Free passage, full salary on voyage. Intermediate leave of 2 months at end of first 21 months, 3 months at end of contract, but 6 months' home leave if re-engaged. Climate healthy, living conditions good. Fully equipped hospital.

Applications in writing, giving full particulars of qualifications and copies of testimonials, to the London Manager, The British Phosphate Commissioners, 2, Grosvenor-gardens, London, S.W.1.

Doctors required to do night calls on a payment-per-call basis, car and medical equipment provided. Excellent opportunity to gain valuable experience in a well-remunerated and congenial appointment.—Please ring REN. 6411 for appointment for interview.

For Residential and Professional purposes: Wimpole-street, third and fourth floors. Lift. C.H., C.H.W. 7 rooms, kitchen and bathroom and cloakroom. Lease 10 years. Rent £750 p.a., exclusive.—Apply sole Agents: ELLIOTT, SON AND BOYTON, 86/87, Wimpole-street, London, W.1. WEL. 8367.

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimens of urine and £2 2s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

Doctors requiring applications, theses copied: Write to MANTON (WESTMINSTER) LTD., 98, Victoria-street, S.W.1 (VIC. 0141), who are specialists.

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4/7